UNIVERSITY OF THESSALY

SCHOOL OF PHYSICAL EDUCATION AND SPORT SCIENCE

PhD Dissertation

Physical activity in depressed patients: A self-determination approach

by

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Submitted in partial fulfillment of the

Requirements for the Degree

Doctor of Philosophy

2017

The approval of the PhD dissertation from the School of Physical Education and Sport Science of University of Thessaly does not imply acceptance of the writer's opinions (Law 5343/32 article 202, par. 2).

Η έγκριση της διδακτορικής διατριβής από τη Σχολή Φυσικής Αγωγής & Αθλητισμού του Πανεπιστημίου Θεσσαλίας δεν υποδηλώνει απαραιτήτως αποδοχή των απόψεων του συγγραφέα (Ν.5343/32 άρθρο 202 παρ.2 – ΦΕΚ 86 / 23-3- 1932).

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Contents

Acknowledgments

Graduating with a doctoral diploma after many years of mainly clinical practice I feel the need to thank those who played a significant role in this long journey.

From a chronological order, I would like to thank the Hippokration Hospital of Thessaloniki for providing me with the opportunity to conduct clinical training in the Child and Adolescent inpatient unit of the Psychiatric Department. Also, many thanks to Zoe N. Winding and Arvid R. Holm from Århus-Denmark for doing their best in my first step towards clinical training away from home. Many thanks to my supervisors in my Masters(MSc) studiesat KULeuven, Belgium, Dr Peter Van de Vliet and Professor Herman Van Coppenolle. I am grateful to Professor Johan Simons from the same University for his trust and support.

Privileged for the unique friendship since my Master studies with my friends, Kathrine Rehder and Gøran Forsgren from Norway, DanielAyalew from Ethiopia, and ErdemGökyaran from Turkey.

I am most grateful to Gene Savelkoul from The Nederlands Paralympic Committee for his exceptional sitting-volleyball trust and mentoring. Many thanks to Gerald Browers from The Netherlands and the World Federation Volleyball for the Disabled for his trust and support. No words to thank my mentor in Paralympic Sports, a legend of the Paralympic Movement and a good friend, Professor Horst Strokhendl from the University of Cologne, Germany. No words to thank Dr Efthymios Motakis from the National University of Singapore inSingapore, a good friend who is always out there for me without a second thought. No words to thank Dr Maria Niskopoulou for being a faithful friend with enormous and unique concern.

I am most grateful to Professor Egil W. Martinsen from the University of Oslo, Norway, a pioneer researcher in the filed of exercise and mental health, and a valuable mentor over the last 15 years. I am most grateful to Professor Marit Sørensen from the Norwegian School of Sport Sciences, Norway, for always trying to do the best for me. More than words can say, Associate Professor Afroditi Stathi from the University of Bath, United Kingdom, a valuable friend in life and a light paradigm of mentoring who is always there for me when I need it, especially in the difficult times. No words to thank Professor Costis Magannaris from the University of Liverpool, United Kingdom, for his unbelievable friendship and mentoring, during the difficult times as well. Many thanks to Professor Patrick Callaghan and to Dr Tim Carter for the unique collaboration in two externally funded research programmes at the University of Nottingham, United Kingdom. Many thanks to Dr Sotirios Koupidis for his concern and support. Many thanks to the library staff of the Gennimatas Hospital in Athens, Greece; Eirini, Dimitra, Artemis, and Evaggelia.

Many thanks to Professor Athanasios Papaioannou from the University of Thessaly, Greece, for granting us with the opportunity to enrich the PhD project with advance equipment. Many and special thanks to the Post Doctoral Fellow Dr Charalampos Krommidasfrom the University of Thessaly for his endless concern and support.

I am most grateful to Professor Dimitrios Ploumpidis from the National and Kapodistrian University of Athens and Director of the Vyron-Kaissariani Community Mental Health Care Centre, Athens, Greece. His trust and support made the recruitment of patients for this doctoral project come true. I am most grateful to Professor Marina Economou from the National and Kapodistrian University of Athens and Director of the Vyron-Kaissarini Community Mental Health Care Centre, who continued to support this Doctoral project as a successor of Professor Dimitrios Ploumpidis. Also, I have no words to thank the staff of this Centre, Alexandros Maridakis and Maria Stamouliwho managed to successfully integrate in their daily schedule a gigantic support to my effort to recruit patients and cope with a series of

difficulties for 29 months in a row. Similarly, I am grateful to Katerina Pikouli and Manolis Loukadakis,who as staff members of the same Centre provided significant support. I am most grateful to psychiatrist Eirhnh Sideri for her absolute and unconditional commitment in supporting patient recruitment, and in dealing with the enormous work of the diagnosis of the patients. Many thanks to Christos Kalatzis and Anastasia Mparouth for the administration support and to psychologists Georgia Kapsi, Pavlina Poulidi, Katerina Fostini, Chrisitna Simoudi, and Anna Kanava for their contribution to patiens' recruitment. Also, I am most grateful to the real protagonists of this doctoral project; the patients who participated in studies 4 and 5, without their contribution the project would not have been completed successfully.

Finally, I have no words to thank the supreme experience of being supervised by my doctoral supervisors; Associate Professor Antonis Hatzigeorgiadis, Assistant Professor Nikolaos Comoutos, and Professor Yannis Theodorakis from the University of Thessaly, Greece.Their absolute commitment to science and to student supervision was the key-factor for the completion of this Thesis and the epitome of working with. I am most grateful to Professor Yannis Theodorakis for his trust and support and for having established a unique Academic frame that I had the amazing opportunity to join in; I consider myself lucky and immensely privileged.
Last but not least, this doctoral Thesis is dedicated to the most important person in my life; my psychoanalysist who has been purifying my personal and professional ingredients.
As Alexander the Great from Greece said almost 2.300 years ago, **«*Στοὺς γονεῖς ὀφείλομεν τὸ ζῆν, στοὺς δὲ διδασκάλους τὸ εὖ ζῆν*»,**we are indebted to our parents for living, but to our teachers for living well.

Ioannis D. Morres, May 2017

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Abstract

The aim of this Thesis was threefold: (i) to contribute to the clarification of the issue of causality between physical exercise and depressionamelioration in adult patients with major depressive disorder (18-65years), (ii) to investigate if self-determination theory (SDT) could revealpredictive properties towards depression relief and physical activity participation in adult outpatients (18-65years) with major depressive disorder, and (iii) to examine whether objectively measured habitual physical activity is associated with predictive effects on the improvement of depression in adult outpatients (18-65years) with major depressive disorder. The first study wasa critical review provided extensive interpretation of the literature referred to exercise for adult patients with major depressive disorder. Based on this study, physical exercise was associated with an improvement in depression, butdepressed patients participating in exercise on prescription schemes documented the highest dropout rates among all patients. Relevant recommendations based on SDT were provided in order to increase treatment effectiveness and to decrease dropout rates. In light of the inconclusive views seen in literature concerning the causal antidepressant effects of exercise, a systematic review was conducted to examineif exercise brings about clinically signficant antidepressant effects on adult patients with major depressive disorder. Based on normative comparisons, exercise led to an improvement in depression that was equivalent to general population. The most effective dose-response relationship was moderate intensity exercise ofthree times per week for both short- or longer-term (3, 8, or 9 weeks). A subsequent systematic review employed practical significance comparisons (meta-analytic techniques) toexploreif the aerobic modality of exercise in particular, compares favourably to routine practice treatment conditions. This meta-analysisfavoured the antidepressant effects of aerobic exerciseattributable to the large and significant overall effect-size and thelow heterogeneity levels. Also, no publication bias was recorded. Coding on participant, intervention, comparison, outcome and design characteristics did not change the result. The most-effective dose-response relationship referred to aerobic exercise of three times per week at moderate intensity for a short- (up to six weeks) or longer period (eight to twelve weeks).Following the supportive evidence for the causal antidepressant effects of exercise, the fourth study of this Thesis investigated the predictive contribution of SDT to depression relief and to physical activity participationin order to provide a robust rationale that could tackle the sedentary lifestyle of depressed patients and the disappointing dropout rates from exercise on prescription schemes. Based on a sample of 206 patients, this study revealed that need satisfaction (competence, autonomy and relatedness) is capable of predicting depression relief

and physical activity participationincluding the corresponding metabolic equivalents by its own right as it overcome and neutralised the positive mediating effects of autonomous-(internal/identified)behavioural regulators(e.g., exercise for pleasure or for personal importance). Depression, however, illustrated an adverse toxic effect on need satisfaction. Controlling forms-(external/introjected)of behavioural regulators(e.g., exercise for external rewards or self-blame) typically comprising the iatrogenic physical activity/exerciseon prescription or promotion model showed no mediating effect.Finally, given that the self-administrative health behavioural pattern of habitual physical activity may represent the front-line treatment tool against depression, the fifth study of this Thesisrecruited 19 depressed patients to explore whether objective habitual physical activity levels measured by means of a 7-day use of triaxial accelerometer devices are associated withantidepressant predictive properties. The study recordedan average of 32 minutes of moderate to vigorous habitual physical activity per day. This amount of habitual physical activitypredicted depression ameliorationand explained 23% of the variance of depression. It should be noted that only 40 seconds of the 32 minutes represented the vigorous component.Collectively, this Thesis has found that physical exercise shows causal antidepressant effects. Also, satisfying the SDT dendrites of psychological needs for exercise may lead to depression relief as well as to participation in physical activity. Finally, the objectively measured level of moderate to vigorous habitual physical activity for 32 minutes per day is related with depression amelioration.Studies 4 and 5 need to be replicated with a longitutinal design in order to draw causal conclusions.Also, the implementation of pragmatic randomized controlled trials is essential in order to translate into real life settings the clinical evidence referred to the antidepresiveness of physical activity/exercise and the predictive power of SDT towards physical activity participation.

Chapter 1. General Introduction

Depression is the most prevalent cause of disturbed mental health that is associated with severe human suffering. Specifically, depression is a life-threatening, disabling and increasingly prevalent mood disorder affecting more than 350 million people worldwide (World Health Organization, 2013). Also, theWorld Health Organization (2008) reports thatdepression is projected to be the leading cause of disease burden worldwide by 2030. To this extent, depression is ranked as a top treatment target (Üstün, 2001). More than 50% of people, after their first episode of depression, will experience at least one additional episode whereas after the second and third episodes, the risk of relapse is increased by70 % and 90%, respectively(Kupfer, 1991).Hence, depression is seen as a chronic condition andlong-term management is required (Richards, 2011), yet only a small number of people will seek treatment for depression; for example only 14% of people in Belgium seek treatment within a year of onset of depression (Bruffaerts, Bonnewyn and Demyttenaere, 2008). Also, depression is related withsevere physical co-morbidity and depressedpeople are twice as likely to die prematurely compared with the general population due to various causes including sedentary-related disorders such as cardiovascular disease (Ösby, Brandt, Correia et al., 2001). Accordingly, both physical and mental health-ensuring interventions on a long-term basis are essential for the treatment of depression.

Major Depressive Disorder

The most common type of depression is major depressive disorder (also called clinical depression), which is typically diagnosed by qualified mental health professionals though structured clinical interviews based on internationally recognized tools including the International Classification of Disease-10 of the World Health Organisation (World Health Organization, 1992) or the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM-5)(American Psychiatric Association, 2013). In addition, major depressive disorder can be diagnosed by means of psychometric tools such as the Patient Health Questionnaire-9 (Spitzer, Kroenke, Williams et al., 1999). Based on the DSM-5, the clinical diagnosis of major depressive disorder is based upon the following criteria: one of the two symptoms, low mood or anhedonia (lack of interest or pleasure) is necessary, in addition to no less than four of the following symptoms: lack of concentration, disturbed sleep, disturbed appetite or weight, fatigue, psychomotor retardation or agitation, feelings of worthlessness,

and persistent thoughts of death or suicide. The symptoms should be present for at least two weeks, and cause impaired functioning.

Depression in Greece

After the onset of the economic crisis in Greece in 2008, the prevalence of depression and the commit suicide rates increased at an alarming rate. Specifically, the one-month prevalence of major depressive disorder has increased from 3.3% in 2008 to 6.8% in 2009, 8.2% in 2011 and 12.3 in 2013 (Economou, Peppou and Souliotis, 2015; Economou, Madianos, Peppou et al., 2013; Madianos, Economou, Alexiou et al., 2011). In adults aged between 35 and 44years, one-month prevalence of major depression is now 16.4% for men and 14.7% for women (Economou, Angelopoulos, Peppou et al., 2016). Also, there has been a substantial increase in the prevalence of suicide ideation and reported suicide attempts (Economou, Madianos, Peppou et al., 2013), whereas the seasonality of suicides in the prefecture of Attica has been strengthened and a noteworthy suicide risk of 96% for suicides by hanging has been recorded (Christodoulou, Efstathiou, Michopoulos et al., 2017). An archival clinical survey conducted by a public hospital in Athens (Sotiria) has found an increase of suicide attempts by 35.71% for the period before (2007) and during the financial crisis (2011) (Stavrianakos, Kontaxakis, Moussas et al., 2013; Stavrianakos, Pachi, Paplos et al., 2013). Further, research has shown that the majority of suicide attempts are mostly associated with mood disorders (Economou, Madianos, Peppou et al., 2013; Fountoulakis, Savopoulos, Siamouli et al., 2013).

In light of the dramatic prevalence of depression, it is noteworthy that waiting times to receive public health services has escalated by more than 200% (Economou, Kaitelidou, Katsikas et al., 2016). Also, the use of mental health services has increased by 120% from 2011 to 2014 (Kentikelenis, Karanikolos, Reeves et al., 2014). In addition, 95% of the urban hospitals face an increase of 10% to 35% in the number of patients presenting in Emergency Services, a significant number of these patients report anxiety problems, depression and stressful situations (Economou, Kaitelidou, Katsikas et al., 2016). Further, a recent phone survey in a sample of 621 households in Athens has recorded additional treatment barriers including social stigma concerns towards widely used treatment forms (Economou, Bergiannaki, Peppou et al., 2016). These concerns included negative stereotypes about antidepressant medication such as addiction problems, altering personality status, and bringing about more harms than benefits. Accordingly, the employment of stereotypical-free

interventions to support routine practice in the treatment of depression appears to be an essential action. Physical exercise is suggested as an important supportive tool.

Physical Exercise and depression

The terms physical exercise and physical activity are often used interchangeably, however, there are distinct differences. According to a classical approach by Caspersen, Powell and Christenson (1985), physical activity is defined as "any bodily movement produced by skeletal muscles that results in energy expenditure (pp.126)", whereas physical exercise is conceptualised as a subset of physical activity "that is planned, structured, repetitive, and purposive in the sense that improvement or maintenance of one or more components of physical fitness is an objective (pp.128) (Caspersen, Powell and Christenson, 1985). To this extent, both terms will not be used interchangeably in the current Thesis but the term physical activity will be used as an umbrella term given that exercise is considered a physical activity subset. However, when clarifications for the subset of exercise become essential, specific reflections will be applied.

Almost 2.500 years ago, the Greek philosopher and physician Hippocrates (460-377 BC) who is considered the father of medicine in the westernized world, recommended physical exercise for the treatment of melancholy (depression). In the modern era, the antidepressant potential of exercise in depressed patients has attracted research attention since the early 1900's when the first promising findings were reported (Franz and Hamilton, 1905; Vaux, 1926). Ever since, various research groups have implemented a series of randomized controlled trials (RCTs) and systematic reviews in depressed people that led to the acknowledgment of the association of exercise with improved depression. As a result of this evidence, since the mid 1990's exercise has been embedded as an antidepressant treatment for patients with mild or moderate depression in the National Health Service in the United Kingdom. In the late 2000's, the European Commission (2008) has released physical activity guidelines regarding the prescription of exercise for health reasons. Guideline-18 stated that *"Public authorities should encourage health insurance schemes to become a main actor in the promotion of physical activity"* and Guideline-19 stated that*"Health insurance schemes should encourage clients to be physically active and should offer financial incentives. Physical activity upon prescription should become available in all EU Member States*.

Consequently, exercise on prescription for health disorders including depression has been embedded in the Health Systems in various European Union member countries but not

in Greece. To the best of the author's knowledge, none of the six elected governments in Greece since the release of the physical activity guidelines in 2008 (European Commission, 2008) has launched an initiative to explore the successful development of exercise on prescription schemes for people with health disorders including depression. As such, depressed outpatients in Greece remain unprivileged with respect to the reductive effects of exercise on depression.

Current Problems in the Literature of exercise and depression

1. Lack of critical reviews on the relationship of exercise with depression

Although critical reviews are prone to bias as they rank moderate in the evidence hierarchy, they represent valuable source of information when they reflect theoretical backgrounds and pragmatic clinical standpoints. A narrative review is capable of formulating a holistic interpretation on the basis of the reviewers' clinical or research experience and available theoretical models (Kirkevold, 1997). Background knowledge, new concepts and various controversies could be integrated in a narrative review with broad coverage and situational choices about the inclusion of evidence (Collins and Fauser, 2005). In light of the lack of critical reviews in the field of exercise and depression, the first step of this Thesis was the implementation of a detailed critical review. This critical review included reflections on self-determination theory (SDT) because self-determined aspects of exercise at that time were (i) attracting increased attention by physical activity guidelines for the treatment of depression (National Institute for Clinical Excellence [NICE], 2009), (ii) revealing more promising potentials with respect to common exercise modelling in cross sectional studies (Sørensen, 2006) and (iii) increasingly employed by a number of clinical RCTs such as by Dunn, Trivedi, Kampert et al. (2005) [see explanation of the preferred intensity in Rimer, Dwan, Lawlor et al. (2012 see pp.99-100)] or by Schuch, Vasconcelos-Moreno, Borowsky et al. (2011).

2. Lack of consensus on the anti-depressiveness of physical exercise

Exercise has been repeatedly associated with depression relief. However, researchers have not reached a consensus on whether this association is causative. The main argument involves consideration that the moderate, large or moderate to large meta-analytic effect-sizes in favour of exercise are often decreased to a small and non-significant effect when coding for trials with higher risk of bias (lower design quality) (e.g., Cooney, Dwan, Greig et al., 2013; Lawlor and Hopker, 2001). On the other hand, however, researchers (Blumenthal and Ong,

2009; Ekkekakis, 2015; Spedding, 2015) have raised serious doubts about a number of the above studies by reporting positive weight and consistency for the exercise and depression literature or by presenting several contradictions in the process of evaluating risk of bias and intervention effects on depression. Moreover, various researchers have provided evidence favouring the causal antidepressant effects of exercise as after coding for risk of bias the effects of exercise remained large and statistically significant (e.g., Robertson, Robertson, Jepson et al., 2012; Schuch, Vancampfort, Richards et al., 2016). In light of the current synthesis of the literature related to exercise for depression, additional research is essential in order to increase further our understanding on whether the link between exercise and depression relief is causative. For this purpose, the current Thesis identified a series of clinical and methodological shortcomings that no previous meta-analytic review has taken into consideration.

A. Risk of bias

The widely known Cochrane risk of bias tool (http://handbook.cochrane.org) is the "all time winner" for evaluating risk of bias in exercise trials for depression. However, it has not been designed for physical therapy interventions such as exercise where double blinding is not possible and dropouts may be a significant issue given the increased motivational demands to exercise participation. Moreover, the Cochrane risk of bias tool has shown reliability problems (e.g., Armijo-Olivo, Ospina, da Costa et al., 2014). In contrast, the PEDro scale is designed for physical therapy interventions, it takes into consideration the issue of dropouts, and it shows high reliability coefficients (Maher, Sherrington, Herbert et al., 2003). However, this scale has been underused in the literature of exercise and depression with one only systematic review (but not meta-analytic) presenting relevant findings (Perraton, Kumar and Machotka, 2010).

B. Depressed patients vs. media responders

All systematic reviews, to the best of the author's knowledge, have included a number of RCTs with samples comprising depressed people who were recruited via media advertisements and had no formal diagnosis of major depressive disorder. Equalizing depressed patients to community volunteers recruited via media responders, however, may reveal shaky conclusions. Community volunteers for exercise trials are typically motivated to exercise trials (Blumenthal and Ong, 2009). Thus, community volunteers may have well-

established motivation to change their lifestyle and built high outcome expectations to the intervention to come. Following these considerations, media responders cannot be considered a convincingly representative segment to depressed patients. Instead, depressed patients have shown severe symptoms of depression and serious psychosocial impairment that led to a mental health service. Also, depressed patients often experience negative feelings of failure or disappointment because mental health services use uncovers the disease severity/complexity and the need for systematic care (Bursztajn and Barsky, 1985; Maguire, Cullen, O'Sullivan et al., 1995; Morgan, 1989). Despite the distinct differences between depressed volunteers recruited through media advertisements and clinically depressed patients recruited through health services, no meta-analytic review, to the best of the author's knowledge, has exclusively focused on RCTs with the latter group.

C. Equalizing depressed adult patients to elderly patients

Across all meta-analytic reviews, researchers have repeatedly included a number of trials with adult patients as well as trials with elderly patients. This is seen as a risky equalization and a significant confound given the distinct differences between adult and elderly depression (Fiske, Wetherell and Gatz, 2009) and the higher depression relief that elderly depressed patients may experience through exercise in comparison to adult patients(Silveira, Moraes, Oliveira et al., 2013). Taking these findings into consideration, a systematic review is needed to clarify the antidepressant effects of exercise exclusively in adult (18-65 years old) depressed patients.

D. Aerobic exercise

It is a common view that aerobic exercise is a convincingly applied exercise intervention in outdoor or indoor settings. Also, it requires minimum or no demands in terms of exercise facilities or sport equipment, and it can be conducted in groups or individually, across both experienced and inexperienced participants in exercise, and in both younger and mature adult patients. Moreover, the aerobic modality of walking is clearly the most pursued type of physical activity among mental health patients (Sørensen, 2006). Despite these benefits, no meta-analytic study has explored the antidepressiveness of aerobic exercise in exclusively clinically depressed adult patients (18-65 years old).

E. Aerobic exercise vs. other types of exercise

Meta-analytic studies stand at the top of evidence-based pyramid. Consequently, they are commonly employed to review trials with depressed patients comparing exercise to a broad range of control conditions including various types of exercise(e.g., Cooney, 2013; Mead, Morley, Campbell et al., 2010; Schuch, Vancampfort, Richards et al., 2016; Schuch, Vancampfort, Rosenbaum et al., 2016). However, various types of exercise such as stretching may also benefit depression (e.g., Jorm, Morgan and Hetrick, 2008; Krogh, Saltin, Gluud et al., 2009; Krogh, Videbech, Thomsen et al., 2012). Hence, the improved depression of control groups assigned to exercise conditions may reduce the effectiveness of exercise interventions and lead to confounding conclusions (Schuch, Morres, Ekkekakis et al., 2016). However, no study, to the best of the author's knowledge, has compared aerobic exercise to control group conditions other than physical exercise exclusively in clinically depressed adult patients.

F. Meta-analytic techniques vs. normative equivalence

Given the likely scenario of the reduced intervention effects by improvements of control groups assigned to exercise conditions with observed benefits on depression, meta-analytic studies may not always be a panacea for drawing firm conclusions. Moreover, meta-analytic techniques (e.g., effect-size calculations) revealing the magnitude of intervention inform only how many standard deviations the post distribution mean of the outcome of interest has shifted from the pre pooled distribution without clarifying if the two distributions still overlap, or if the second distribution shifted to the normal population range. Thus, researchers need to consider alternative methods to practical significance analysis. Clinical significance analysis instead, excludes the methodological weaknesses of practical significance analysis (e.g., meta-analytic techniques) by measuring effect through normative comparisons (Cribbie and Arpin-Cribbie, 2009). In detail, clinical significance analysis provides information about the magnitude of the effect by clarifying via normative comparisons if patients' symptoms (intervention or control group's symptoms separately) shifted from being within the dysfunctional range to being within a nomothetically average range. In this manner, it illustrates recovery coefficients from depression. Collectively, clinical significance analysis excludes replication of previously confounded findings derived from practical significance analysis and provides recovery coefficients enabling result interpretation from a clinically meaningful perspective.

G. The sedentary lifestyle of outpatients with major depressive disorder

Despite the depression reducing effects of exercise, it is widely acknowledged that depressed patients show a sedentary lifestyle. Also, when attempting to participate in exercise on prescription programmes in the community, they reveal the highest dropout rates among all referral groups (e.g., Crone, Johnston, Gidlow et al., 2008; Murphy, Raisanen and Moore, 2010).These findings, however, are in contrast to reports indicating that mental health patients (including depressed patients) show high preferences for exercise as a treatment modality (Fleischmann, 2003; Sigurdsson, Ólafsdóttir and Gottfredsson, 2008; Ussher, Stanbury, Cheeseman et al., 2007) and high motivation upon prescription endorsement (Crone, Johnston, Gidlow et al., 2008; Harrison, McNair and Dugdill, 2005). It is thus seen that the sedentary lifestyle or the decline in the initial motivation or positive predisposition might deal with ineffective or irrelevant processes of motivational activation to the profile of depressed people.

To this extent, the widely used iatrogenic consultancy that aims to increase exercise participation by treating motivation as a uni-dimensional health-oriented construct seems to be an insufficient strategy. Instead, self-determination theory (SDT)(Deci and Ryan, 1985; Ryan and Deci, 2017)postulates that motivation is a multidimensional construct and the adoption of health behavioural patters is a complex phenomenon involving multifaceted motivational sequences that interplay with basic psychological needs.

SDT regards human nature from an antithetic position in comparison to the definition of the depressed state of human nature. In particular, depression is a state of human nature that is characterized by anhedonia, lack of interest and pleasure that lead to apathy towards any “activation” for personal development and health gains. SDT, however, regards people as active organisms with inherent and deeply evolved tendencies toward psychological growth and development (Ryan and Deci, 2000). This lifespan propensity is evident in the phenomenon of intrinsic motivation where novelty, challenges and opportunities are sought on grounds of interest, pleasure, or satisfaction for the shake of the activity itself, and in the phenomenon of internalization where social practices are integrated. Although these growth tendencies underlying intrinsic motivation and internalization are evolved and therefore natural, their robust operation depends on the satisfaction of specific psychological components by supportive social agents. These components are the three basic psychological needs of competence, autonomy and relatedness, which refer to, respectively, mastering personally challenging tasks, operating in the absence of outside controls, and experiencing meaningful social interaction during behavioural performance (Deci & Ryan, 1985).

When psychological needs are not satisfied, intrinsic motivation, which ensures the most self-determined behavioural regulator, is thwarted and other type(s) of motivation may prevail across the continuum of motivation. These types of motivation include amotivation that refers to a deactivated(or lack of) motivation towards behaviour. Departing from this negative edge of the continuum of motivation, SDT subsequently places extrinsic types of motivation. These include the (i) external type of motivation where behavioural performance is highly controlling and regulated on the basis of gaining rewards, fulfilling commitments or avoiding pressure,and (ii) introjected type of motivation where behavioural performance is also controlling and regulated through feelingsof self-criticism or guiltor shame relief efforts. The least extrinsic type of motivation across the continuum is the identified motivation where behavioural performance is regulated in order to achieve goals of personal value. Overall, the continuum of motivation includes deactivated motivation, namely amotivation, and develops through extrinsic types of motivation to intrinsic types of motivation.

Collectively, the higher the needs satisfaction, the more likely the motivation is to be internally regulated and the more internally regulated, the stronger the motivation, and the more likely is engagement in the behaviour(Ryan and Deci, 2000). As a behavioural point of reference regarding how people place themselves in relationship to physical activity or inactivity, Stage of Change Theory (SOCT) (Prochaska and Diclemente, 1983)is valuable methodological approach as itis capable of capturing both currently performed or unperformed, and prospectively performed or unperformed stages of physical activity behaviour. In detail, SOCT comprises five potential stages. These include the stages precontemplation (do not think to exercise), contemplation (intent to exercise in the next six months), preparation (intent to exercise in the immediate future), action (have started exercising in the past six months) and maintenance (have sustained exercising in the last six months).

Up to date, no research has investigated as to how the sedentary lifestyle of depressed outpatients could be tackled. However, there is a promising, yet limited and only partially relevant to depressed outpatients,body of evidence for tackling physical inactivity in mental health settings. This evidence stems from two studies;one using the framework of SDT(Sørensen, 2006)and one using the framework of SDT in combination with SOCT(Vancampfort, Moens, Madou et al., 2016). Both studiesshowed promising results for the unresolved issue of low exercise participation among mental health patients.

In particular, in a sample of mental health outpatients with various diagnoses, Sørensen (2006) treated motivation in line to SDT as a multidimensional continuum

comprising the state of amotivation, and extrinsic and intrinsic regulators. Sørensen (2006) computed a logistic regression analysis and found that extrinsic regulation including external, introjected and identified regulators outlining health-oriented aspects for exercise based on, respectively, rewards, self-criticism or personal importance (e.g., I was told to exercise by others, I ought to exercise, exercise is good for my health,) did not predict exercise participation. In contrast, intrinsic regulation where exercise participation dealt with interest, pleasure, fun, or the shake of the activity itself showed a strong predictive power. Also, intrinsic motivation correlated with lower illness symptoms during physical activity, whereas extrinsic motivation showed an adverse relationship with physical activity.

Also, in a sample comprising patients with affective disorders including bipolar depression and major depressive disorder, Vancampfort, Moens, Madou et al. (2016) employed SDT as well as the SOCT(Prochaska and Diclemente, 1983) to examine behavioural regulation along the continuum of motivation across the stages of change for exercise.Findings showed that different behavioural regulators prevailed across the various stages of exercise participation. Specifically, higher autonomous regulation (identified and intrinsic regulators indexed together) and lower amotivation levels were found in the action and maintenance stages in comparison to the pre-preparation stage. Also, lower levels of external regulation were seen in the action compared to pre-preparation stage. Similarly, lower levels of introjected regulation were recorded in the action and maintenance stages in comparison to pre-preparation stage. Based on these findings, higher levels of autonomous regulation are found in sustained exercise participation whereas higher levels of external and introjected regulations are seen in physical inactivity or at the stage where intentions to exercise participation are formulated. Finally, introjected regulation showed a negative contribution to the between-groups variability, specifically between the preparation and maintenance stages indicating that motivation to exercise dealing with feelings of self-guilt portray patients with a sedentary lifestyle or with early-shaped (and potentially premature) intentions to exercise participation.

Nevertheless, the findings by Sørensen (2006) and Vancampfort, Moens, Madou et al. (2016) are not fully relevant to the scope of this Thesis dealing with outpatients with major depressive disorder. Although Sørensen (2006) did recruit outpatient participants, these participants had mixed diagnoses and almost 80% showed a certain amount of physically active. Also, Vancampfort, Moens, Madou et al. (2016) recruited mainly inpatient (83%) and physically active (66%) participants including a significant number (42%) of bipolar

depressed patients. Further, Vancampfort, Moens, Madou et al. (2016) factored in physically inactive patients not indenting to exercise or intending to exercise in the next six months into one variable namely pre-preparation due to a limited number of physically inactive patients.

In addition, neither Sørensen (2006) nor Vancampfort, Moens, Madou et al. (2016) employed the SDT tenets of psychological needs. Thus, the relationship of behavioural regulation with the three psychological needs of competence, autonomy and relatedness was not investigated. This is an important research area because SDT suggests that the more these needs are satisfied the more likely the motivation is to be internally regulated. The more internally regulated, the stronger the motivation, and the more likely is engagement in the behaviour in question. Further, Sørensen (2006) andVancampfort, Moens, Madou et al. (2016)did not employ outcome measures of depression, thus it remains unexplored ifbehavioural regulators as well as psychological needs are associated with depression. Therefore, exploration of the interplay among psychological needs, behavioural regulators, physical activity and depression becomes essential.

Finally, both studies come from countries with embedded physical activity services in the mental health system in contrast to the Greek primary mental health care system. This consideration leads to speculations that the samples in the studies of Sørensen (2006) andVancampfort, Moens, Madou et al. (2016), who were predominantly physically active, might have more well-established and/or different cognitive schemes in relationship to physical activity as a result of professional psycho-education and not as a result of mass media inputs or self-administrated processes that Greek patients might hold.

Collectively, the current trends in literature stress the importance of an SDT-based study in combination to SOCT theory to build on and expand the previous work of Sørensen (2006) and Vancampfort, Moens, Madou et al. (2016) in order to explore motivational pathways towards exercise participation by addressing, however, the following innovative approaches:(i) the inclusion of exclusively major depressed adult outpatients (18-65years old), (ii) data collection in the Greek primary mental health care system where physical activity/exercise on prescription is not an available treatment option, (iii) the employment of the SDT tenets of psychological needs, and (iv) the employment of outcome measures of depression.

Aims

The purpose of this Thesis was threefold: to (a) systematically review the current literature in order to advance our understanding on the relationship between physical exercise and decreased levels of depression, (b) examine motivational modellingthat may contribute to decreased levels of depression and to physical activity participation and (c) investigate if objective measures of habitual physical activity could predict depression relief.

The first purpose was realised by critically reviewing the current trends seen in the literature andby exploring the causal effects of exercise on depression relief via systematic reviews with novel standpoints that excluded previous confounders. To that end, three different reviews were conducted. The first review employed a critical overview and interpretation, reflecting on SDT, of the current trends in the literature of exercise and depression. The second review was a systematic review that employed the innovative approach of clinical significance analysis via normative comparisons in order to investigate whether exercise leads to an improvement in depression that is equivalent to general population. In the third systematic review, a meta-analytic study employed a novel approach by examining ifthe aerobic modality of exercise in particular provides higher antidepressant effects when compared to routine practice treatment conditions.

Both systematic reviews involved elucidation of the optimum dose-response relationship between exercise and depression. Also, both systematic reviews adopted two additional novel standpoints: (i) evaluation of risk of bias with the PEDro scale (ii) reviewing only RCTs with exclusively clinically depressed adults aged 18-65 years old with a diagnosis of major depressive disorder who were recruited via health services and not via media advertisements.

The second purpose of this Thesis was to explore a rationale in order tackle the sedentariness of major depressed adult outpatients by discovering potential pathways of motivation to physical activity participation. To this extent, a field study grounded on the SDT premises examined the association of psychological needs and behavioural regulation with depression and physical activity in a purposefully selected sample of 206 major depressed adult outpatients. To the best of the author’s knowledge, no similar research endeavour has been previously applied. The thirdpurpose of this Thesis, not previously implemented,was to examine the association of objective levels of habitual physical activity with depression. Therefore, a study with a purposefully recruited sample of 19 clinically depressed adult outpatients investigated whether objective habitual physical activity measured

via a 7-day triaxial accelerometers use is capable of providing antidepressant predictive effects.

Research Questions

a. The lack of critical reviews on the relationship of physical exercise with depression provided the impetus to address the first research question of what is the critical interpretation of and the relevant recommendations derived from the current trends in the literature of exercise with depression.

b. In light of the deficits of practical significance analysis and the lack of consensus on the causal antidepressant effects of exercise in clinically depressed adult patients, the second research question was whether physical exercise brings about clinically significant antidepressant effects in exclusively clinically depressed adult patients.

c. Given the unexplored antidepressant impact of the aerobic modality of exercise in comparison to routine practice treatment conditions in exclusively clinically depressed adult patients, the third research question was whether the aerobic modality of exercise in particular compares favourably to routine practice treatment conditions for the above target group.

d. In light of the encouraging findings ofSDT-based studies on motivational pathways towards exercise participation among mental health patients, the fourth research question was whether SDT premisesdescribingbehavioural regulation and psychological needs could reveal associations with physical activity and depression in exclusively clinically depressed adult outpatients.

e. Taking into consideration the lack of objective measures of habitual physical activity levels in exclusively clinically depressed adult outpatients, the fifth research question was whether objectivehabitual physical activity levels measured through accelerometer devices could predict depression relief.

Chapter 2. Study 1

Physical exercise and major depressive disorder in adult patients

Abstract

This chapter provides an understanding of physical exercise as a treatment modality for adult patients diagnosed with major depression as a primary disorder. The profile of major depressive disorder is defined, and evidence derived from clinical trials for the antidepressant effect of physical exercise is presented. Also, the most effective exercise protocols are identified. Finally, recommendations are provided as to how exercise consultancy in depressed patients could be applied in order to increase motivation and participation rates in exercise on referral programs endorsed by general practitioners (GPs) and realized in the pragmatic setting of routine practice in the community.

Introduction

A case study illustrating the association of physical exercise with depression relief has been presented byVan de Vliet, Vanden Auweele, Knapen et al. (2004). Specifically, Louis (pseudonym) is a 32-year-old male patient with major depressive disorder, repeatedly admitted to hospital within a 3-year period. At the latest admission (lasted 164 days), Louis' severity of depression was mild-moderate (score of 17 on the Beck Depression Inventory [BDI])(Beck, Rush, Shaw et al., 1979). At day 20, fitness training was added to medication and cognitive-behavioral therapies, and consisted of stationary cycling, treadmill walking/running, and resistance exercises delivered in small groups for 45 minutes, 3 days per week for a period of 20 weeks. Fitness training was associated with more positive emotional and behavioral responses compared to medication; Louis felt fit, enjoyed himself, and received enough support with regards to fitness training. Fitness training was also associated with positive changes in various aspects of Louis' functioning including enhanced coping strategies, sustained efforts to continue activities, and improved awareness of physical well-being. This experience was combined with a reduction of .75 standard deviation in depression, measured daily during the fitness-training program on a 7-item scale. At discharge, Louis' depression improved from mild-moderate into mild (BDI score of 13) (Van de Vliet, Vanden Auweele, Knapen et al., 2004).

Major depressive disorder

Depression is a serious mental health disorder that causes severe human suffering and in the worst case ends with suicide. Apart from being a lethal disorder, depression is also an independent risk factor to other disorders, like cardiovascular disorders, and it is associated with substantial reduction in lifetime expectancy. Moreover, depression is a psychosocially disabling disorder. In the United Kingdom, a study by the London School of Economics(Layard, 2006)reports that depression explains a significant portion of theunemployment variance as 40 per cent of all incapacity benefits are given to people with mental illness. To this extent, it is unsurprising that depression has been identified since the mid 1990s as the leading cause of disability worldwide and the second top contributor to the global health burden of disease by the year of 2020(Murray and Lopez, 1997; Murray, Lopez and Organization, 1996). As a consequence, the World Health Organization has ranked depression as a top treatment target (Üstün, 2001).

Together with anxiety and substance misuse disorders, depressive disorders are the most common mental disorders, and major depressive disorder (MDD) is the most common. According to the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, DSM-IV(American Psychiatric Association, 2000), MDD has the following diagnostic criteria. One of the two symptoms, low mood or anhedonia (lack of interest or pleasure) is necessary, in addition to no less than four of the following symptoms: lack of concentration, disturbed sleep, disturbed appetite or weight, fatigue, psychomotor retardation or agitation, feelings of worthlessness, and persistent thoughts of death or suicide. The symptoms should be present for at least two weeks, and cause impaired functioning. Epidemiological studies indicate that 16 per cent of the population in the United States will meet criteria for MDD across the lifespan, with women being almost two times more vulnerable than men(Kessler, Berglund, Demler et al., 2003). Given that MDD is the most common type of depression, the term depression and MDD will be used interchangeably in the current chapter.

The severity of depression is psychometrically assessed by means of self- as well as clinician-rated measures. The Beck Depression Inventory-IIand the Hamilton Rating Scale for Depression (HAMD-17) (Hamilton, 1960) are the most common self- and clinician-rated measures, respectively.

The classical treatment forms of depression are medication and various modes of psychotherapy. These forms of treatment, however, are often seen as costly, not easily accessible, not always effective, time-consuming, and are associated with social stigma. Medication may have unpleasant side effects, and dropout rates may be high. Moreover, almost 50 per cent of depressed people do not take medication as prescribed, and thus cannot benefit accordingly. Furthermore, the classical treatment forms cannot meet the increased physical health needs of depressed patients. In general, depressed patients show a sedentary unhealthy lifestyle, including cigarette smoking, unhealthy nutrition and physical inactivity, leading to low levels of physical fitness. To this extent, depression is associated with increased levels of mortality and premature death rates. The physical health aspect of depression is an important therapeutic consideration due to the fact that prolonged psychiatric hospitalization is inversely related to the poor physical health of the depressed patients(Schubert, Yokley, Sloan et al., 1995).

As a consequence, inexpensive, easily accessible, and cost-effective antidepressant interventions that ensure physical health benefits are essential to support the classical treatment forms of depression. Physical exercise is a valuable adjunct on account of the aforementioned qualities.

The antidepressant effect of physical exercise

The Greek philosopher and physician Hippocrates (460-377 BC), widely recognized as the father of medicine in the Western civilization, recommended physical exercise for the treatment of melancholy (depression). In the modern era, Franz and Hamilton (1905) and (Vaux, 1926)and were pioneer researchers in the field of physical exercise and depression, and were the first to report on the positive effects of physical exercise on depression.

Ever since, a limited number of randomized controlled clinical trials (RCTs) and controlled clinical trials (CTs) have been conducted on adult patients diagnosed with major depressive disorder as a primary disorder, and referred by health services. However, all of the trials have repeatedly indicated the association of physical exercise with antidepressant effect. Specifically, eight RCTs have compared aerobic exercise favorably or equally to other exercise modalities or traditional psychiatric interventions. Aerobic exercise was more effective than stretching(Knubben, Reischies, Adli et al., 2007), low intensity and relaxation(Bosscher, 1993), and similarly effective to relaxation, yoga and stretching(Veale, Le Fevre, Pantelis et al., 1992b). Compared to traditional treatments, aerobic exercise was equally effective to time limited or unlimited psychotherapies(Greist, Klein, Eischens et al., 1979), and more effective than occupational therapy(Martinsen, Medhus and Sandvik, 1985) psychotherapy and antidepressants(Veale, Le Fevre, Pantelis et al., 1992a), antidepressants(Pilu, Sorba, Hardoy et al., 2007), antidepressants and electroconvulsive therapy (ECT) (Schuch, Vasconcelos-Moreno, Borowsky et al., 2011). In two CTs, aerobic exercise compared favorably to psychotherapy and antidepressants(Bosscher, Van Tilburg and Mellenbergh, 1997) and antidepressants(de la Cerda, Cervelló, Cocca et al., 2011).

The antidepressant effect of aerobic exercise was recorded in both self- and clinician-rated outcome measures. Seven trials(Bosscher, Van Tilburg and Mellenbergh, 1997; Greist, Klein, Eischens et al., 1979; Knubben, Reischies, Adli et al., 2007; Pilu, Sorba, Hardoy et al., 2007; Schuch, Vasconcelos-Moreno, Borowsky et al., 2011; Veale, Le Fevre, Pantelis et al., 1992a; Veale, Le Fevre, Pantelis et al., 1992b) used clinician-rated, and three(Bosscher, 1993; de la Cerda, Cervelló, Cocca et al., 2011; Martinsen, Medhus and Sandvik, 1985) used self-rated primary outcomes of depression. As a consequence, the alleviation of depression through aerobic exercise is confirmed by the patients as well as by the clinicians.

Patients showed a wide range of severity classifications; treatment-resistant (Pilu et al., 2007), normal-mild(Bosscher, 1993), moderate(Bosscher, 1993; de la Cerda, Cervelló, Cocca et al., 2011; Knubben, Reischies, Adli et al., 2007), moderate-severe(Greist, Klein, Eischens et al., 1979; Martinsen, Medhus and Sandvik, 1985; Veale, Le Fevre, Pantelis et al., 1992a;

Veale, Le Fevre, Pantelis et al., 1992b), severe(Pilu, Sorba, Hardoy et al., 2007; Schuch, Vasconcelos-Moreno, Borowsky et al., 2011),and non-medicated(Bosscher, 1993; Greist, Klein, Eischens et al., 1979)depressed patients. Noteworthy, non-medicated(Bosscher, 1993; Greist, Klein, Eischens et al., 1979), and treatment-resistant depressed patients(Pilu, Sorba, Hardoy et al., 2007) challenge health professional practice(Beesley and Mutrie, 1997; Shelton and Papakostas, 2008). It seems therefore, that aerobic exercise could be an effective strategy in depression management at different levels of depression severity.

Both indoor and outdoor aerobic exercise protocols were found, and were mainly delivered in supervised group sessions. Indoor (clinic community or hospital gym); aerobic exercise in equipment-based supervised conditions delivered in community gym in groups(Pilu, Sorba, Hardoy et al., 2007)or individually in hospital gym (Knubben, Reischies, Adli et al., 2007; Schuch, Vasconcelos-Moreno, Borowsky et al., 2011). Outdoor (park); group-based and supervised aerobic exercise(de la Cerda, Cervelló, Cocca et al., 2011; Martinsen, Medhus and Sandvik, 1985; Veale, Le Fevre, Pantelis et al., 1992a; Veale, Le Fevre, Pantelis et al., 1992b). Outdoor (park); aerobic exercise(Bosscher, Van Tilburg and Mellenbergh, 1997; Bosscher, 1993)on the basis of individual induction and group supervision(Bosscher, 1993), and individual supervision(Bosscher, Van Tilburg and Mellenbergh, 1997). It is not clear if fitness gains are associated with higher depression relief because of the limited number of studies taking relevant measures. However, when fitness measures were taken, aerobic exercise resulted in fitness gains (increases in the maximum work capacity [Vo2max]) and higher antidepressant effect than both antidepressant medication and psychotherapy(Bosscher, Van Tilburg and Mellenbergh, 1997; Veale, Le Fevre, Pantelis et al., 1992a), or occupational therapy(Martinsen, Medhus and Sandvik, 1985).

Two of the reviewed RCTs examined if the degree of adherence to the exercise program influenced the antidepressant effect of aerobic exercise. Aerobic exercise showed equal antidepressant effect to yoga, relaxation and stretching(Veale, Le Fevre, Pantelis et al., 1992b), and higher effect to psychotherapy and antidepressants(Veale, Le Fevre, Pantelis et al., 1992a)in patients with 100 per cent as well as >50 per cent adherence rates to the exercise program.

Most studies have addressed the effect of adding exercise to other forms of treatment, as both the exercise and control group patients in the majority of trials were on concurrent treatments including antidepressants and psychotherapy(Veale, Le Fevre, Pantelis et al., 1992a; Veale, Le Fevre, Pantelis et al., 1992b), antidepressants and sleep-deprivation(Knubben, Reischies, Adli et al., 2007), non-medicated care (Bosscher, 1993;

Greist, Klein, Eischens et al., 1979), antidepressants and ECT(Schuch, Vasconcelos-Moreno, Borowsky et al., 2011), antidepressants(de la Cerda, Cervelló, Cocca et al., 2011; Pilu, Sorba, Hardoy et al., 2007), and occupational therapy (Martinsen, Medhus and Sandvik, 1985).

A direct comparison between aerobic exercise and a placebo was not controlled by any of the reviewed trials. Indirect evidence, however, provides optimistic findings in favor of aerobic exercise. First, the higher antidepressant effect of exercise compared to psychotherapy was seen in groups with similar outcome expectations(Bosscher, Van Tilburg and Mellenbergh, 1997). Second, the effect of aerobic exercise against equal or less effective types of exercise was seen in two (Knubben, Reischies, Adli et al., 2007; Veale, Le Fevre, Pantelis et al., 1992b)of five RCTs. The latter finding decreases further placebo speculations for aerobic exercise. These speculations were derived from the disappointment of the unimproved, in terms of depression, control group that was not assigned to the aerobic exercise intervention(Bosscher, 1993). Finally, the higher effect of aerobic exercise compared to stretching remained significant after controlling for the influence of parallel treatments (antidepressants/sleep-deprivation)(Knubben, Reischies, Adli et al., 2007).

The reviewed trials, although demonstrating a positive effect to aerobic exercise on depression, have methodological deficits in the design, conduct, analysis, and reporting. These deficits include lack of intention-to-treat analyses, blinded assessor, random allocation, concealed allocation, and/or baseline imbalance in outcome measures between the intervention and control group. In addition, few studies have adequate follow-up assessments. Given that higher risks of bias are associated with larger treatment effects(Schulz, 2001; Schulz, Chalmers, Hayes et al., 1995), the reviewed trials were classified on the basis of top methodological qualities. To this extent, trials fulfilling most of the aforementioned methodological quality criteria were analyzed in terms of the exercise protocols and the involved dose-response relationship. In this manner, conclusions are drawn from trials with more robust designs. Examples are presented below.

In addition, to provide students or practitioners of routine practice with clarified findings on how to apply physical exercise in practice, we carried out a clinical taxonomy on the reviewed trials by separately grouping those with either inpatients or outpatients.

Exercise in practice

In this section examples will be given on how exercise could be effectively delivered to depressed patients. In the first RCT(Knubben, Reischies, Adli et al., 2007), the exercise dose included daily supervised and individual interval training for 30 minutes. Inpatients

exercised for ten days, in a hospital gym. In each session, inpatients walked five times for a period of three minutes at an intensity corresponding to a lactate concentration of three mmol/l in capillary blood and a heart rate of 80 per cent of the maximum. After each workload, inpatients walked at half speed for three minutes to rest.

In the second RCT(Pilu, Sorba, Hardoy et al., 2007) the exercise dose included supervised group-based interval training that consisted of two sessions of 50 minute-aerobic training per week for eight months on their preferred choice of 20 cardio-fitness machines. Patients selected a different cardio-fitness machine every four minutes. The exercise sessions took place in a hospital.

In the third RCT(Schuch, Vasconcelos-Moreno, Borowsky et al., 2011) the exercise dose included aerobic exercise three times per week for three weeks at a preferred intensity (provided that 16kcal/kg/week was completed). Inpatients exercised on an individual and supervised mode in a hospital gymnasium on equipment-based, preferred exercises of stationary bicycle, treadmill or elliptic.

In the last RCT with depressed inpatients(Martinsen, Medhus and Sandvik, 1985), the exercise dose included a 60-minute aerobic session at the intensity of 50-70 per cent of the Vo2max, three times per week for nine weeks. Inpatients exercised under supervision in a park, in small groups using walking and jogging. This was supplemented, to a limited extent, with bicycling or swimming at their preference.

Finally, only one reviewed trial (CT) recruited depressed outpatients(de la Cerda, Cervelló, Cocca et al., 2011). The exercise dose included aerobic exercise three times per week for eight weeks at low intensity. Outpatients were women, exercised in one group under supervision in a hospital gymnasium, using fun dance, low impact aerobic gymnastics, and walking. The use of three types of exercise suggests that a number of depressed patients participated in preferred type(s) of exercise, especially since the latter type of exercise (walking) is preferred by the majority of mental health patients.

Collectively, the exercise dose included three sessions per week for eight(de la Cerda, Cervelló, Cocca et al., 2011), nine(Martinsen, Medhus and Sandvik, 1985), or three(Schuch, Vasconcelos-Moreno, Borowsky et al., 2011)weeks at the low-moderate intensity of 50-70 per cent of the maximum work capacity (Vo2max), aligning with the national and international physical activity recommendations. The corresponding exercise protocols of these trials reflected on preferred type or intensity of exercise. In addition, both short-term aerobic exercise protocols (ten days) and long-term exercise protocols (eight months)(Knubben, Reischies, Adli et al., 2007; Pilu, Sorba, Hardoy et al., 2007) provided

antidepressant effects. The latter exercise protocol also reflected the patients' preferences regarding the type of exercise. Examples of exercise protocols are presented in Appendix 1.

Physical exercise and depressed patients in primary care

In the reviewed trials, depressed inpatients showed encouraging low dropout rates ranging from 0 to 27 per cent. In one study of outpatients, no dropout was seen(de la Cerda, Cervelló, Cocca et al., 2011); this is an encouraging result because depressed outpatients often show disappointing dropout rates when they are referred by GPs to exercise on referral scheme programs (these programs last 12-14 weeks, and are realized in public or private leisure facilities). In particular, mental health referrals (consisting mainly of depressed outpatients) show the lowest adherence rates in the uptake (adoption-first actual exercise session) and completion (maintenance) stages amongst all referral groups. In detail, they show the lowest uptake rates of all health referral groups(D' Silva, 2006; Stathi, Milton and Riddoch, 2006) lower uptake than physical health referrals (60% vs. 69%, $p<0.001$)(Crone, Johnston, Gidlow et al., 2008), lower completion rates than physical health referrals (>80% attendance; 22% vs. 34%)(Crone et al., 2008), and the lowest completion rates of all health referrals(D' Silva, 2006; Dugdill, Graham and McNair, 2005; Stathi, Milton and Riddoch, 2006).Also, the evaluation of an exercise referral scheme in Wales, in the UK, reports that mental health referrals were less likely to adhere to and complete the program than physical health referrals (Murphy, Raisanen and Moore, 2010).

A typical explanation to this problem indicates that a-motivation is the predominant symptom of the depressed patients. However, some studies have shown that mental health patients, including depressed patients, valued exercise, and evaluated it as more appealing than other therapies(Fleischmann, 2003; Sigurdsson, Ólafsdóttir and Gottfredsson, 2008; Ussher, Stanbury, Cheeseman et al., 2007). These positive findings are supported by studies on the preceding referral stages to the uptake and completion stages. Specifically, in the stages between the referral endorsement by the GP and the attendance of the first exercise referral scheme appointment with the exercise consultant, the mental health referrals appear to be highly motivated; in comparison to physical health referrals, mental health referrals represented the top predictor to exercise attendance uninfluenced by GP related factors (e.g., distance from the surgery, etc), and scored the top attendance rate at thefirst exercise referral scheme appointment(Harrison, McNair and Dugdill, 2005). Also, fewer mental health than physical health referrals (six per cent vs. 10 per cent) dropped-out between the referral endorsement and the first appointment(Crone, Johnston, Gidlow et al., 2008) despite the four

to six week delay between services(Stathi, Milton and Riddoch, 2006). Hence, the stage of the first exercise referral scheme appointment with the exercise consultant appears to be the crucial cross-point that signifies: 1) the decrease of the initial motivation of the depressed patients in the preceding stage of the referral endorsement, 2) the increase of the dropout rates of the depressed patients in the subsequent stages of the uptake and completion of the exercise program.

Consultancy aims to motivate the patient to uptake, and complete the exercise on referral program. The motivation is described by the way it is regulated on a continuum from lack of motivation (a-motivation) through externally controlled regulation (external, introjected and identified) to internally controlled motivation (integrated and intrinsic). Consultancy is often medically oriented, aiming to enforce the patients' motivation to take up and complete the exercise program on the basis of extrinsically controlled regulation. Extrinsically regulated motivation includes motives of external ("I exercise because I was told by my doctor or others"), introjected ("I ought to exercise for my health") and identified ("I exercise to obtain health benefits") orientation.

According to Self-Determination Theory (SDT)(Deci and Ryan, 1985) the regulation of the patient's motivation will be affected by the degree of satisfaction of three basic psychological needs through the activity. The psychological needs are the needs for competence, autonomy, and relatedness. They are defined as follows: 1) competence is a sense of mastery and the perception of being effective in executing the behavior, 2) autonomy refers to an internal locus of control and the perception that the behavior is self-selected, 3) relatedness is the satisfied involvement with others and a sense of belonging. The more these needs are satisfied, the more likely the motivation is to be internally regulated. The more internally regulated, the stronger the motivation, and the more likely is engagement in the behavior in question. This has been documented to be the case also with psychiatric patients (with mixed diagnoses)(Sørensen, 2006). Internally regulated physical activity motives gave higher odds ratios for being physically active. There was also a relationship between intrinsically regulated motivation and the experience of symptom reduction during exercise(Sørensen, 2006). Thus, recommendations will be given as to how exercise consultancy could be structured to address intrinsically motivated exercise participation.

Recommendations on exercise consultancy

Intrinsic motivation is generated through a self-determined behavior on the basis of interest, pleasure, and fun, implemented for the sake of the activity itself rather than an external reason such as commitments or rewards. Intrinsic motivation is realized within a

secure environment, belonging and responsive to initiations social milieu to ensure relatedness. Intrinsic motivation is catalyzed with competence enforcement via optimal challenges, and effectance promoting feedback (approval and agreement with an appropriate action) to subjects responsible enough for the competent performance to feel autonomy; while competence is necessary for any type of motivation, perceived autonomy is required for the motivation to be intrinsic(Ryan and Deci, 2000; Ryan and Deci, 2000). Noteworthy interventions that provide synergetic and not individual support for the needs of autonomy, relatedness, and competence go hand in hand with greater engagement in the behavior(Deci, Eghrari, Patrick et al., 1994).

The practical applications of this knowledge for exercise consultants are thus:In order to make the motivation more intrinsically regulated it is important to try to satisfy the three basic needs (for autonomy, competence and relatedness) through the engagement in physical activity. To achieve this, relevant techniques are suggested. Details can be found in Appendix 2.

Appendix 1. Examples of exercise protocols for depressed patients

A. Examples of exercise protocols in depressed outpatients

1. Intervention: 3 x 45 minutes per week for 8 weeks, supervised cardiovascular exercises in a group that aimed at increasing heart rate and lung function. Duration was gradually increased to 60 minutes. Protocol consisted of warm-up, low impact aerobic gymnastics, fun dance and walking oriented exercises to cardiovascular, and cool down work. The location was a hospital gymnasium. No dropouts were seen. All patients were prescribed antidepressants. Depression (BDI) improved from moderate into minimal-mild(de la Cerda, Cervelló, Cocca et al., 2011).

B. Examples of exercise protocols in depressed inpatients

1. Intervention: Three times per week for three weeks on self-selected exercise modality (stationary bicycle, treadmill, or elliptic) as well as on self-selected intensity exercise provided that 16Kcal/kg/week would be completed. Location was at university hospital. No dropouts were seen. All patients were prescribed antidepressants, and a limited number (six per cent) were prescribed electroconvulsive therapy. Depression (HAMD-17) was improved from severe to normal(Schuch, Vasconcelos-Moreno, Borowsky et al., 2011).

2. Intervention: 3 x 60 minutes per week for 9 weeks, supervised jogging and walking in groups. The location was a park. Exercises were supplemented by bicycling and swimming according to the patient's preference. Intensity was set at 50-70 per cent of the maximum work capacity (Vo2max), measured at baseline. Duration was gradually increased to 60 minutes. Dropouts were 14%. All patients were prescribed to psychotherapy and occupational therapy. A third of the patients were prescribed antidepressants. Depression (BDI) improved from moderate-severe to mild-moderate(Martinsen, Medhus and Sandvik, 1985).

3. Intervention: Three minutes interval-aerobic individual walking, five times a day for 10 days at a mean intensity corresponding to a lactate concentration of 3mmol/l in capillary blood and to 80 per cent of the maximum heart rate. Three-minute bouts were undertaken at half-speed between workloads. Gradual increases in treadmill elevation to maintain intensity. Supervisor provided feedback on walking techniques, muscle complaints, amount of exertion. Location was in university hospital. No dropouts were seen. The majority of the patients were prescribed antidepressants, and a third of the patients sleep-deprivation. Depression (Bech-Rafaelsen Melancholy Scale-BRMS) was improved from moderate to mild(Knubben, Reischies, Adli et al., 2007).

4. Intervention: Sixty minutes/two times week/32 weeks, 5 minutes warm up, 50 minutes training on a self-selected cardio-fitness machine, switching every 4 minutes (20 machine options). Five minute cooling down/stretching. Inpatients exercised in groups and supervised. The location was a hospital gym. No dropouts were seen. All patients were prescribed antidepressants. Depression (HAMD-17) was improved from severe to mild(Pilu, Sorba, Hardoy et al., 2007).

Appendix 2. Presentation of techniques towards the enforcement of psychological needs

1. Give autonomy support: provide options, support own initiatives, provide positive feedback, enforce self-selection, participants take part in decisions, create internal locus of control. 2. Support experience of competence: optimal challenges, approval when appropriate, stimulate self-efficacy, avoid providing rewards or mentioning external benefits, avoid judgmental approaches, utilize instructions for safety reasons only. 3. Support relatedness; promote non-competitive types of activities, enforce positive and mastery oriented climate, work on social support and relationships, create feelings of belonging to group.

Chapter 3. Study 2

Physical exercise, dose-response relationship, and clinically depressed adult patients. A systematic review and normative comparisons

Abstract

This study aimed at reviewing exercise trials with clinically depressed adults, focusing on the optimum dose-response relationship between exercise and clinical depression. An electronic/manual literature search was conducted. Eligible trials were assessed for post-intervention depression comparability to a normal population at the 0.5, 1.0, and 1.5 standard deviation (SD) intervals via equivalence testing, and for methodological quality with the Physiotherapy Evidence-Based Database Scale (8=top quality). The optimum dose-response relationship was investigated towards the most conservative interval (0.5SD) in trials with higher methodological quality scoring (≥5). Fourteen eligible trials were found. All trials employed aerobic exercise. In seven trials, exercise reduced post-intervention scores of depression to an equivalent interval to a normal population. In three trials with higher quality scoring (6, 5, and 5), exercise of 45-60min at low-moderate intensity 3 times/week for 3, 8, or 9 weeks reduced post-depression to the 1.5SD, 0.5SD, and 1.0SD intervals compared to a normal population, respectively. Short and longer-term low-moderate intensity aerobic exercise of 45-60min for 3 times/week involving, partially, patients' preferred mode/intensity exercise improved depression to a comparable state to a normal population. The limited number/quality of reviewed trials hinders definite conclusions about the optimum dose-response relationship between exercise and clinical depression.

Introduction

Physical exercise of 3 times per week for a period of 10-14 weeks is prescribed to depressed adult patients as an antidepressant treatment strategy attributable to the established association with improvement in depression (National Institute for Clinical Excellence [NICE], 2009). Over the last 20 years, however, researchers have not reached a consensus on if this association is causal. Based on epidemiological causality criteria (Hill, 1965; Mausner and Kramer, 1985), some reviews support a causal link (Biddle and Mutrie, 2008; Mutrie, 2000) in contrast to other reviews with less optimistic views (Arent, Rogers and Landers, 2002; Dishman, 1995; O'Neal, Dunn and Martinsen, 2000). Also, meta-analyses from late 1990's early 2000's, found large effect-sizes (ESs) for exercise (Craft and Landers, 1998; Lawlor and Hopker, 2001), the latter study, however, claimed for exaggerated ES by the poor number/quality of the clinical trials. More recent meta-analyses reported that the significantly large (Josefsson, Lindwall and Archer, 2014; Mead, Morley, Campbell et al., 2010), moderate to large (Kvam, Kleppe, Nordhus et al., 2016), moderate (Cooney, Dwan, Greig et al., 2013; Rimer, Dwan, Lawlor et al., 2012) or small to moderate (Krogh, Nordentoft, Sterne et al., 2011) for exercise were reduced to moderate (Josefsson, Lindwall and Archer, 2014; Mead, Morley, Campbell et al., 2010), or to small (Cooney, Dwan, Greig et al., 2013; Krogh, Nordentoft, Sterne et al., 2011; Kvam, Kleppe, Nordhus et al., 2016; Rimer, Dwan, Lawlor et al., 2012) and not significant after coding for risk of bias.

However, researchers (Blumenthal and Ong, 2009; Ekkekakis, 2015; Spedding, 2015) have raised serious doubts about a number of the above unoptimistic studies by reporting the positive weight and consistency of the literature for the therapeutic value of exercise or by presenting significant flaws as to how the unfavourable comparisons for exercise were extracted from. Further, other recent meta-analyses found significantly moderate to large(Silveira, Moraes, Oliveira et al., 2013) or large (Robertson, Robertson, Jepson et al., 2012; Schuch, Vancampfort, Richards et al., 2016) ESs for exercise. Moreover, in the latter two studies, the large ESs were uninfluenced or relatively uninfluenced after coding for risk of bias as they remained steady large (Schuch, Vancampfort, Richards et al., 2016) or became moderate-large (Robertson, Robertson, Jepson et al., 2012) and stayed significant.

In line, meta-analyses with separate evaluations on trials with clinically diagnosed samples found significantly moderate (Cooney, Dwan, Greig et al., 2013), or large (Craft and Landers, 1998; Rethorst, Wipfli and Landers, 2009; Schuch, Vancampfort, Richards et al., 2016) ESs for exercise. Moreover, in two studies the large ESs remained steady large (Schuch,

Vancampfort, Richards et al., 2016) or became even larger (Rethorst, Wipfli and Landers, 2009) and remained significant after coding for risk of bias.

To this extent, the optimum dose-response relationship between exercise and improved depression that can be derived from the literature is subject to various conclusions. Two reviews report that exercising for 10-16 or 9-12 weeks is more effective than exercising for 4-9, or 8 or less weeks. (Craft and Landers, 1998; Rethorst, Wipfli and Landers, 2009). Other reviews report the opposite (Krogh, Nordentoft, Sterne et al., 2011). Also, exercising 5 times/week rather than 2-4 times/week seems to be more effective (Rethorst, Wipfli and Landers, 2009). However, adherence seems not to be a significant moderator in other studies (Krogh, Nordentoft, Sterne et al., 2011). Exercise for 45-59min shows larger effects than 30-44min or ≥60min, (Rethorst, Wipfli and Landers, 2009) however, some reviews suggest that exercise of <20, 21-30, 31-45 or >46min shows no differences in effect (Craft and Landers, 1998). Also, different exercise modes are equally effective (Craft and Landers, 1998; Rethorst, Wipfli and Landers, 2009), but aerobic exercise(Schuch, Vancampfort, Richards et al., 2016; Silveira, Moraes, Oliveira et al., 2013), resistance or combined aerobic/resistance (Mead, Morley, Campbell et al., 2010) might have larger effects. Further, various intensities seem to be equally effective (Craft and Landers, 1998; Rethorst, Wipfli and Landers, 2009), but light-moderate intensity shows large effects and moderate to vigorous intensity small and non-significant effects (Cooney, Dwan, Greig et al., 2013). Finally, some reviews suggest outdoor exercise is more effective (Craft and Landers, 1998) while other reviews report larger effects for indoor exercise (Robertson, Robertson, Jepson et al., 2012).

In light of the current synthesis of the literature, it is noteworthy that no review has focused exclusively on trials with adult clinically depressed patients aged 18-65 years old recruited via health services. Particularly, reviews are typically including a number of trials with depressed community volunteers recruited via media advertisements or a number of trials with elderly or with mixed elderly and adult samples. This could be seen as an important gap in the literature due to a threefold reason. First, there are distinct differences between adult and elderly depression (Fiske, Wetherell and Gatz, 2009). Second, elderly samples seem to experience higher depression relief through exercise compared to adult samples(Silveira, Moraes, Oliveira et al., 2013). Third, depressed patients are disheartened and experience severe clinical manifestations as well as disappointment or frustration by the necessity to systematically use mental health services (Bursztajn and Barsky, 1985; Maguire, Cullen, O'Sullivan et al., 1995; Morgan, 1989). In contrast, community volunteers for exercise trials are typically motivated to exercise (Blumenthal and Ong, 2009), may have experienced sub-

syndromal symptoms and built well-established outcome expectations or determination to lifestyle change. Another unexplored aspect in literature involves consideration that no meta-analytic review has evaluated trials' risk of bias with a standardized tool that is designed for physical therapy interventions such as physical exercise.

This evaluation appears to be essential as systematic errors of bias may be related not only with overestimated intervention effects (Moher, Pham, Jones et al., 1998; Schulz, 2001; Schulz, Chalmers, Hayes et al., 1995) but also with intervention specific design flaws. Finally, it is widely known that no exercise review for depression has explored the magnitude of the exercise effect via an approach other than the meta-analytic technique of ES, which is a typical approach of the practical significance analysis. The ES, however, informs only how many standard deviations (SDs) the post distribution mean of the outcome of interest has shifted from the pre pooled distribution without clarifying if the two distributions still overlap or if the second distribution shifted to the normal population range. Clinical significance analysis instead, provides information about the magnitude of the exercise effect by clarifying via normative comparisons whether patients' symptoms shifted from being within the dysfunctional range to being within a nomothetically average range (Cribbie and Arpin-Cribbie, 2009).

Apart from providing recovery coefficients from depression, clinical significance analysis may also serve as an alternative to the methodological weaknesses that practical significance analysis may show when exploring the anti-depressiveness of exercise. Specifically, practical significance analysis such as meta-analytic techniques cannot capture the true antidepressant effect of exercise interventions when control groups are assigned to exercise conditions with observed benefits to depression (e.g., Krogh, Saltin, Gluud et al., 2009; Krogh, Videbech, Thomsen et al., 2012). Although clinical significance analysis has been employed to assess the antidepressant effects of traditional therapies (Nasiakos, Cribbie and Arpin-Cribbie, 2010), it remains understudied in the exercise-depression literature.

Taking all findings into consideration, this study aimed at reviewing clinical exercise trials in clinically depressed adult patients with a focus on the optimum dose-response relationship by assessing the clinical significance of the antidepressant effect of exercise and by controlling for methodological qualities.

Methods

After approval by the Ethics Committee of the University of Thessaly, this study employed the checklist of the Preferred Reporting Items for Systematic Reviews and Meta-

Analyses (PRISMA) statement in order to systematically review the literature (Moher, Liberati, Tetzlaff et al., 2009).

Inclusion criteria

Studies were considered as eligible for inclusion via the PICOS criteria (participants, intervention, comparison, outcome, and study design): i) participants aged 18-65 recruited via health services with a referral for depression or with a diagnosis of major depression as a primary disorder without psychotic features, and not as a result of a medical disorder/condition, ii) exercise interventions as defined by the American College of Sports Medicine (Swain and Brawner, 2012), iii) comparison of exercise interventions to other treatments, no treatment, placebo, waiting list, or other types of exercise, iv) depression as the primary outcome measure, and v) studies with a clinical trial design.

Literature search

Literature search included the MEDLINE, PsycINFO, Embase, ISI Web of Science, SPORTDiscus, and the PEDro databases for studies written in English language and published in peer reviewed journals. The search covered the period from January 1980 to March 2016. Keywordsof "clinical*" "depress*", "major", "disorder", "refer*", "patient", or "adult" AND "exercise", "aerobic", "strength", "anaerobic", "training", or "run*" were employed. To avoid publication bias, the ProQuest Dissertations and Theses database was searched to locate unpublished trials. Hand-searching was used to screen references lists. Most authors of the eligible trials were contacted to provide additional information. Fisher test computation controlled for between-group differences in the number of patients who i) dropped-out and ii) were on concurrent treatment forms.

Risk of bias

Internal validity qualities were evaluated with the Physiotherapy Evidence-based Database scale (PEDro) (Maher, Sherrington, Herbert et al., 2003) to record systematic errors of bias that favour overestimation of the intervention effect. The PEDro scale is a comprehensive measure of methodological quality with good psychometric properties (de Morton, 2009; Macedo, Elkins, Maher et al., 2010; Maher, Sherrington, Herbert et al., 2003), widely used in physical therapy (Bhogal, Teasell, Foley et al., 2005; Brown, Huedo-Medina, Pescatello et al., 2011; Knols, de Bruin, Shirato et al., 2010), and in various research areas lately (Pan, Wang, Xie et al., 2014; Pinto, Maher, Ferreira et al., 2012). Criteria 2-11 assess

internal validity that lead to a maximum score of 10 by allocating two points for between-groups comparisons and point estimates/variability measures, three points for blinding patients/therapists/assessors, two points for random/concealment allocation, and three points for baseline balance, intention-to-treat, and <15% drop-out rates. The maximum score in this study was set to be 8, deducting the two points for blinding, as it is difficult, if not impossible, to blind patients/therapists in exercise trials for depressed patients. An independentresearcher assessed the methodological quality of each trial, and sought consensus with the author's evaluations onthe relevant evaluations. Cohen's Kappa statistic was computed, and interpreted based on the Landis and Koch (Landis and Koch, 1977) reference to estimating the inter-rater agreement (0.81-1.0, 0.61-0.80, 0.41-0.60, 0.21-0.40, 0.0-0.20 and <0, as nearly perfect, substantial, moderate, fair, slight and poor, respectively).

Clinical significance analysis

The antidepressant effect of exercise was assessed via the clinical significance analysis. This analysis compared the scores of the studied populations to those of the normal population in order to record if patients' average depressive symptoms shifted from being within the dysfunctional range to being within a nomothetically average range (Cribbie, Gruman and Arpin-Cribbie, 2004; Kendall, Marrs-Garcia, Nath et al., 1999; Rogers, 1993; Schuirmann, 1987; Seaman and Serlin, 1998). For this purpose, general population norms of the primary outcome for each trial were allocated. Analysis was conducted based on the method of Cribbie and Arpin-Cribbie (Cribbie and Arpin-Cribbie, 2009). First, a two independent-samples difference-based test, the heteroscedastic t-test (Welch, 1938), explored if the baseline mean of depression levels of the reviewed sample was significantly higher compared to the normal comparison group mean. Conditional on the significant difference identified in the previous step, the heteroscedastic, two independent-sample, Schuirmann-Welch equivalence test (Gruman, Cribbie and Arpin-Cribbie, 2007) explored if the post-treatment mean of reviewed sample was equivalent to the normal comparison group mean. The reviewed sample was seen as equivalent to a normal population if the difference between the means fell within an equivalence interval. Equivalence intervals were set at the 1.5SD, 1.0SD, and 0.5SD levels of the normative group. The latter SD level (0.5) stands for the most conservative equivalence interval indicating the highest proximity to a state of normalcy (Cribbie and Arpin-Cribbie, 2009).

The optimum dose-response relationship

The optimum dose-response relationship was investigated by combining the PEDro and the clinical significance analysis results. Specifically, trials with aerobic exercise showing antidepressant effects equivalent to a normal population were hierarchically classified on the basis of top methodological quality scoring. In this manner, the most-effective dose-response relationship towards the top conservative equivalence interval (0.5SD) was identified in trials with a score of ≥5 on the PEDro scale that corresponds to higher methodological quality scoring.

Results

Search results

The literature search is illustrated in the flow chart (Figure 1). Fourteen trials (Bosscher, Van Tilburg and Mellenbergh, 1997; Bosscher, 1993; de la Cerda, Cervelló, Cocca et al., 2011; Krogh, Saltin, Gluud et al., 2009; Krogh, Videbech, Thomsen et al., 2012; Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Mutrie, 1986; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Schuch, Vasconcelos-Moreno, Borowsky et al., 2011; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015; Veale, Le Fevre, Pantelis et al., 1992a; Veale, Le Fevre, Pantelis et al., 1992b) were eligible for inclusion.

Characteristics of eligible trials

Participants

Participants were outpatients (Bosscher, Van Tilburg and Mellenbergh, 1997; de la Cerda, Cervelló, Cocca et al., 2011; Krogh, Saltin, Gluud et al., 2009; Krogh, Videbech, Thomsen et al., 2012; Mota-Pereira, Silverio, Carvalho et al., 2011; Mutrie, 1986; Rueter, 1980; Veale, Le Fevre, Pantelis et al., 1992a; Veale, Le Fevre, Pantelis et al., 1992b) or inpatients (Bosscher, 1993; Martinsen, Medhus and Sandvik, 1985; Pilu, Sorba, Hardoy et al., 2007; Schuch, Vasconcelos-Moreno, Borowsky et al., 2011; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) with mild (Bosscher, 1993), moderate (de la Cerda, Cervelló, Cocca et al., 2011; Krogh, Videbech, Thomsen et al., 2012; Martinsen, Medhus and Sandvik, 1985; Mutrie, 1986; Rueter, 1980) moderate-severe (Veale, Le Fevre, Pantelis et al., 1992a; Veale, Le Fevre, Pantelis et al., 1992b) moderate and treatment resistant (Krogh, Saltin, Gluud et al., 2009), severe and treatment resistant (Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007), or severe (Bosscher, Van Tilburg and Mellenbergh, 1997; Schuch,

Vasconcelos-Moreno, Borowsky et al., 2011; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) depression.

Intervention characteristics

All trials employed aerobic exercise as the intervention format. In a double arm trial (Krogh, Saltin, Gluud et al., 2009), the second intervention format was strength training. Individual or group, as well as supervised or unsupervised aerobic exercise protocols were found in both outdoor or indoor settings.

Indoor settings*:* individual/supervised running in a sport track (Rueter, 1980), and individual/supervised (Pilu, Sorba, Hardoy et al., 2007; Schuch, Vasconcelos-Moreno, Borowsky et al., 2011; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) or group/supervised (Krogh, Saltin, Gluud et al., 2009) equipment-based aerobic exercise in a clinic gym. *Outdoor settings:* group/supervised aerobic exercise (Martinsen, Medhus and Sandvik, 1985; Veale, Le Fevre, Pantelis et al., 1992a; Veale, Le Fevre, Pantelis et al., 1992b) and individual/supervised (Bosscher, Van Tilburg and Mellenbergh, 1997), or individual induction and group/supervised (Bosscher, 1993) running in a park. *Outdoor or home-based settings:* unsupervised walking sessions, complemented by an indoor-(clinic) individual/ supervised treadmill session (Mota-Pereira, Silverio, Carvalho et al., 2011), unsupervised aerobic exercise (individual or with others at the patient's preference) and 20-30min individual fitness consultation biweekly (Mutrie, 1986). *Outdoors and indoors:* group/supervised aerobic exercise in a gym and in a park (de la Cerda, Cervelló, Cocca et al., 2011). *Undefined settings:* group/supervised exercise on a stationary cycle ergometer (Krogh, Videbech, Thomsen et al., 2012).

Aerobic exercise as a complementary intervention. Seven trials employed aerobic exercise complementary to antidepressants and psychotherapy (Krogh, Saltin, Gluud et al., 2009; Veale, Le Fevre, Pantelis et al., 1992b), non-medicated care (Bosscher, 1993), counselling (Rueter, 1980), antidepressants(de la Cerda, Cervelló, Cocca et al., 2011; Pilu, Sorba, Hardoy et al., 2007), and occupational therapy supported by psychotherapy and antidepressants (Martinsen, Medhus and Sandvik, 1985). Five trials employed aerobic exercise complementary to treatment as usual (TAU) consisted of antidepressants and psychotherapy (Veale, Le Fevre, Pantelis et al., 1992a), antidepressants (Bosscher, Van Tilburg and Mellenbergh, 1997; Mota-Pereira, Silverio, Carvalho et al., 2011) or antidepressants and electroconvulsive therapy (ECT) (Schuch, Vasconcelos-Moreno, Borowsky et al., 2011; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015). Across the above twelve trials, 100%, 70%-80%, and ≤45% of the aerobic groups were prescribed

antidepressants in four (de la Cerda, Cervelló, Cocca et al., 2011; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Schuch, Vasconcelos-Moreno, Borowsky et al., 2011), two (Krogh, Saltin, Gluud et al., 2009; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) and four (Bosscher, Van Tilburg and Mellenbergh, 1997; Martinsen, Medhus and Sandvik, 1985; Veale, Le Fevre, Pantelis et al., 1992a; Veale, Le Fevre, Pantelis et al., 1992b) trials, respectively. The aerobic groups also received more concurrent treatments in three trials (Martinsen, Medhus and Sandvik, 1985; Rueter, 1980; Veale, Le Fevre, Pantelis et al., 1992a) and included more patients on antidepressants in one trial (Veale, Le Fevre, Pantelis et al., 1992b) than the control groups. Finally, all but four control groups (Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Schuch, Vasconcelos-Moreno, Borowsky et al., 2011) were receiving concurrent treatments.

Aerobic exercise as a mono-intervention*:* In two trials aerobic exercise was employed as mono-intervention (Krogh, Videbech, Thomsen et al., 2012; Mutrie, 1986) and was compared to stretching (Krogh, Videbech, Thomsen et al., 2012) or to a combination of stretching and strengthening exercises or to waiting list (for exercise consultancy). In these two trials the control groups were receiving no concurrent treatment.

Drop-outs*:* The intervention and the control groups did not show statistically significant differences in the number of patients who dropped out. Details are presented in Table 1.

Comparison of intervention modes

Compared to psychiatric treatments, aerobic exercise was more effective than counselling (Rueter, 1980), antidepressants (de la Cerda, Cervelló, Cocca et al., 2011; Pilu, Sorba, Hardoy et al., 2007), occupational therapy supported by psychotherapy and antidepressants (Martinsen, Medhus and Sandvik, 1985), and TAU consisted of psychotherapy and antidepressants (Bosscher, Van Tilburg and Mellenbergh, 1997; Veale, Le Fevre, Pantelis et al., 1992a), antidepressants and ECT (Schuch, Vasconcelos-Moreno, Borowsky et al., 2011; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) or antidepressants (Mota-Pereira, Silverio, Carvalho et al., 2011).

In comparison to other exercise modes, aerobic exercise showed higher effectthan low intensity training combined with relaxation and breathing exercises (Bosscher, 1993), and similar effect to low intensity exercise comprising relaxation, stretching and yoga (Veale, Le Fevre, Pantelis et al., 1992b) as well as to relaxation (Krogh, Saltin, Gluud et al., 2009). In the

latter trial, the second intervention arm of strength training showed equal effects to relaxation (Krogh, Saltin, Gluud et al., 2009).

When aerobic exercise was employed as a mono-intervention, it was compared to other exercise modes showing equal effects to stretching (Krogh, Videbech, Thomsen et al., 2012), and higher effects than waiting-list (for exercise consultancy) or stretching and strength exercises (Mutrie, 1986).

Aerobic exercise and placebo*:* No trial compared aerobic exercise with placebo to examine if outcome expectations had an impact on depression. One trial that compared aerobic exercise favourably to TAU, measured outcome expectations in a non-standardised process (Bosscher, Van Tilburg and Mellenbergh, 1997). The trial did not find between-group differences, suggesting no placebo effects for aerobic exercise.

Aerobic exercise and adherence rates*:* The equal effect of aerobic exercise to other exercise modes including relaxation (Krogh, Saltin, Gluud et al., 2009), or low intensity exercise (Veale, Le Fevre, Pantelis et al., 1992b), and its higher effect compared to TAU (Mota-Pereira, Silverio, Carvalho et al., 2011; Veale, Le Fevre, Pantelis et al., 1992a), was observed in patients with both 100% or >50% adherence to exercise protocol.

Aerobic exercise and fitness gains*:* When aerobic exercise resulted in statistically significant increases in maximum work capacity (Vo2max), its antidepressant effect compared equally to relaxation (Krogh, Saltin, Gluud et al., 2009), or stretching (Krogh, Videbech, Thomsen et al., 2012), and favourably to TAU (Bosscher, Van Tilburg and Mellenbergh, 1997; Veale, Le Fevre, Pantelis et al., 1992a) or to occupational therapy (Martinsen, Medhus and Sandvik, 1985). Details are presented in Table 1.

Outcome measures

Nine trials (Bosscher, Van Tilburg and Mellenbergh, 1997; Krogh, Saltin, Gluud et al., 2009; Krogh, Videbech, Thomsen et al., 2012; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Schuch, Vasconcelos-Moreno, Borowsky et al., 2011; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015; Veale, Le Fevre, Pantelis et al., 1992a; Veale, Le Fevre, Pantelis et al., 1992b) and five trials (Bosscher, 1993; de la Cerda, Cervelló, Cocca et al., 2011; Martinsen, Medhus and Sandvik, 1985; Mutrie, 1986; Rueter, 1980) used clinician-rated and self-rated primary outcomes of depression, respectively (Table 2). The clinician-rated outcomes included the Clinical Interview Scale (Goldberg, Cooper, Eastwood et al., 1970) in two trials (Veale, Le Fevre, Pantelis et al., 1992a; Veale, Le Fevre, Pantelis et

al., 1992b), and the Hamilton rating scale for Depression (Hamilton, 1960) in six trials (Bosscher, Van Tilburg and Mellenbergh, 1997; Krogh, Saltin, Gluud et al., 2009; Krogh, Videbech, Thomsen et al., 2012; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Schuch, Vasconcelos-Moreno, Borowsky et al., 2011). The self-rated outcomes included the Self-rating Depression Scale (Zung, 1965) in one trial (Bosscher, 1993), and the Beck Depression Inventory (Beck, Ward, Mendelson et al., 1961) in four trials (de la Cerda, Cervelló, Cocca et al., 2011; Martinsen, Medhus and Sandvik, 1985; Mutrie, 1986; Rueter, 1980).

Study design

All trials were designed as clinical trials.

Risk of bias:Three trials reached the top scores of 8 (Schuch, Vasconcelos-Moreno, Borowsky et al., 2011; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) or 7 (Krogh, Videbech, Thomsen et al., 2012) on the PEDro scale, three trials the score of 6 (Krogh, Saltin, Gluud et al., 2009; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007), three trials the score of 5 (Bosscher, Van Tilburg and Mellenbergh, 1997; de la Cerda, Cervelló, Cocca et al., 2011; Martinsen, Medhus and Sandvik, 1985), and five trials the score of 4 (Bosscher, 1993; Mutrie, 1986; Rueter, 1980; Veale, Le Fevre, Pantelis et al., 1992a; Veale, Le Fevre, Pantelis et al., 1992b) (Table 2). Allocation concealment, intention-to-treat, and assessor blinding were unfulfilled by eight (Bosscher, 1993; Martinsen, Medhus and Sandvik, 1985; Mutrie, 1986; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Schuch, Vasconcelos-Moreno, Borowsky et al., 2011; Veale, Le Fevre, Pantelis et al., 1992a; Veale, Le Fevre, Pantelis et al., 1992b), six (Bosscher, 1993; Mota-Pereira, Silverio, Carvalho et al., 2011; Mutrie, 1986; Rueter, 1980; Veale, Le Fevre, Pantelis et al., 1992a; Veale, Le Fevre, Pantelis et al., 1992b), and eight (Bosscher, 1993; Martinsen, Medhus and Sandvik, 1985; Mutrie, 1986; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Schuch, Vasconcelos-Moreno, Borowsky et al., 2011; Veale, Le Fevre, Pantelis et al., 1992a; Veale, Le Fevre, Pantelis et al., 1992b) randomized controlled trials (RCTs), respectively. Also, assessor blinding, concealed and random allocation were unfulfilled by two trials (Bosscher, Van Tilburg and Mellenbergh, 1997; de la Cerda, Cervelló, Cocca et al., 2011). Due to the latter unfulfilled criterion the two trials were identified as controlled trials (CTs). Cohen's Kappa statistic was 0.62, indicating a substantial inter-rater reliability on the PEDro scoring (Landis and Koch, 1977).

Clinical significance analysis

Aerobic exercise brought about a decrease in depression that was equivalent to the general population norms (Aasen, 2001; Campo-Arias, Diaz-Martinez, Eduardo et al., 2006; Sanz, Perdigón and Vázquez, 2003; Seggar, Lambert and Hansen, 2002; Zimmerman, Chelminski and Posternak, 2004a) at the 1.5SD, 1.0SD, and 0.5SD intervals in seven (Bosscher, Van Tilburg and Mellenbergh, 1997; Bosscher, 1993; de la Cerda, Cervelló, Cocca et al., 2011; Martinsen, Medhus and Sandvik, 1985; Mutrie, 1986; Rueter, 1980; Schuch, Vasconcelos-Moreno, Borowsky et al., 2011), four (de la Cerda, Cervelló, Cocca et al., 2011; Martinsen, Medhus and Sandvik, 1985; Mutrie, 1986; Rueter, 1980), and one trial (de la Cerda, Cervelló, Cocca et al., 2011), respectively. The methodological quality scoring of these trials was 4 (Bosscher, 1993; Mutrie, 1986; Rueter, 1980), 5 (Bosscher, Van Tilburg and Mellenbergh, 1997; de la Cerda, Cervelló, Cocca et al., 2011; Martinsen, Medhus and Sandvik, 1985), and 8 (Schuch, Vasconcelos-Moreno, Borowsky et al., 2011). In all but one trial (Mutrie, 1986), aerobic exercise was employed as a complementary intervention. Details are presented in table 3.(Veale, Le Fevre, Pantelis et al., 1992a)

The dose-response relationship

Of the seven trials where aerobic exercise brought about an antidepressant effect equivalent to a normal population, two RCTs (Martinsen, Medhus and Sandvik, 1985; Schuch, Vasconcelos-Moreno, Borowsky et al., 2011), and two CTs (Bosscher, Van Tilburg and Mellenbergh, 1997; de la Cerda, Cervelló, Cocca et al., 2011) showed a higher methodological scoring on the PEDro scale (≥5), in particular a score of 8 (Schuch, Vasconcelos-Moreno, Borowsky et al., 2011), and 5 (Bosscher, Van Tilburg and Mellenbergh, 1997; de la Cerda, Cervelló, Cocca et al., 2011; Martinsen, Medhus and Sandvik, 1985).

In the RCT with a score of 8 (Schuch, Vasconcelos-Moreno, Borowsky et al., 2011), a dose of 3 times/week/3weeks at a preferred intensity corresponding to at least 16kcal/kg/week resulted in depression scores reduction that was equivalent to a normal population at the 1.5SD interval. Participants were severely depressed inpatients, exercised individually/supervised at low-moderate intensity for 45min on average in a hospital gymnasium following an equipment-based exercise protocol, and were able to select their preferred exercise mode out of three options (stationary bicycle, treadmill or elliptic); no patient dropped out.

In the RCT with a quality score of 5 (Martinsen, Medhus and Sandvik, 1985), the dose of 3 times/week/9weeks of 60min at low-moderate intensity (50-70% Vo2max) decreased

depression to equivalent level to a normal population at the 1.0SD interval. Participants were moderately depressed inpatients. They exercised in a park, in small groups and under supervision on walking and jogging, supplemented by bicycling or swimming at their preference. The drop-out rate was <15%.

In the CT with a quality score of 5 (de la Cerda, Cervelló, Cocca et al., 2011), the dose of 3 times/week/8weeks of 45min at moderate intensity resulted in depression scores reduction that was equivalent to a normal population at the 0.5SD. Participants were moderately depressed female outpatients, who exercised, in a gym and in a park, in one group and under supervision on fun dance, aerobic gymnastics, and walking. The inclusion of three exercise modes might have satisfied personal preferences for exercise modes. The drop-out rate was 5%.

In the second CT with a quality score of 5 (Bosscher, Van Tilburg and Mellenbergh, 1997), the dose of 1 time/week/12weeks of interval running at moderate intensity on average brought about an improvement in depression that was equivalent to a normal population at the 1.5SD. Participants were severely depressed inpatients, who exercised individually in a public park under supervision (co-running) in weeks 1 to 3 or 4. They were instructed to select their preferred intensity in order to avoid speeding up breathing rhythm to an unpleasant level or causing other unpleasant conditions. Patients performed additional exercise sessions, but the exact content/number was unreported, making the interpretation of the findings difficult. No drop-outs were reported.

Discussion

The most effective dose-response relationship between aerobic exercise and clinical depression identified in this review indicated that three sessions per week for 45-60min at low-moderate intensity, in a supervised and mainly group-based format for 3 (Schuch, Vasconcelos-Moreno, Borowsky et al., 2011), 8 (de la Cerda, Cervelló, Cocca et al., 2011), or 9 (Martinsen, Medhus and Sandvik, 1985) weeks led to an improvement in depression that was equivalent to a normal population at the 1.5SD (Schuch, Vasconcelos-Moreno, Borowsky et al., 2011), 1.0SD (Martinsen, Medhus and Sandvik, 1985) and 0.5SD (de la Cerda, Cervelló, Cocca et al., 2011) intervals. The 0.5SD and 1.5SD intervals point out the most and least proximal level, respectively, to a state of normalcy (Cribbie and Arpin-Cribbie, 2009). Hence, the most effective dose-response relationship brought about treatment changes within the nomothetically average range. The importance of our findings, however, is somehow moderated by the methodological flaws of these trials including unfulfilled random (de la

Cerda, Cervelló, Cocca et al., 2011) or concealment allocation and assessor blinding (de la Cerda, Cervelló, Cocca et al., 2011; Martinsen, Medhus and Sandvik, 1985).

The most effective dose-response relationship involved patients' preferences. Particularly, patients chose the exercise modality (from three options) and intensity provided that 16kcal/kg/week would be completed (Schuch, Vasconcelos-Moreno, Borowsky et al., 2011), they attended a small number of exercise sessions based on extra modalities such as swimming or cycling at their preference (Martinsen, Medhus and Sandvik, 1985), or they exercised on three modalities presumably satisfying part of their preferences (de la Cerda, Cervelló, Cocca et al., 2011). Although pragmatic research examining the impact of exercise on depressed patients in routine practice is limited (Schuch, Morres, Ekkekakis et al., 2016), the available evidence has related preference-based exercise with better outcomes compared to prescribed-based (conventional) exercise in exercise on referral facilities. These outcomes included better depression, self-esteem, or quality of life in depressed patients (Callaghan, Khalil, Morres et al., 2011) and lower drop-out rates (in patients with mixed diagnoses including depression) (Morton, Biddle and Beauchamp, 2008). Thus, preference-based exercise emerges as a promising strategy in exploring the optimum dose-response relationship. This strategy warrants further investigation (Morres, Stathi, Martinsen et al., 2014). Noteworthy, preference-based exercise compared to conventional-based exercise shows better outcomes also in various studies with general population segments (Hamlyn-Williams, Freeman and Parfitt, 2014; Rose, 2007).

This review has various strengths. Publication bias was decreased due to allocation of unpublished RCTs. Also, in contrast to previous exercise reviews for depression, only clinical trials with depressed adult patients were reviewed given that elderly depression in comparison to adult depression may show a different clinical profile (Fiske, Wetherell and Gatz, 2009) and a higher improvement through exercise(Silveira, Moraes, Oliveira et al., 2013). Further, only clinical trials with patients referred by health professionals were reviewed, whereas most reviews typically include a number of trials that recruit people via study advertisements. Media respondents, however, cannot be assumed to be similar to referred patients as they might be motivated to change their lifestyle and might have well-defined outcome expectations. Referred patients instead, will have experienced a serious disturbance that led to a health service, and the referral process may often cause negative feelings as it uncovers the disease severity/complexity as well as the necessity for systematic care (Bursztajn and Barsky, 1985; Maguire, Cullen, O'Sullivan et al., 1995; Morgan, 1989). Our findings are, therefore, of particular importance to clinical practice, especially since the demonstrated efficacy of the

most effective dose-response relationship was seen in trials where aerobic exercise was employed as an add-on intervention (apart from the trial of Mutrie), was compared to treatment as usual or to active control conditions (psychiatric therapies) and was conducted in both indoor or outdoor exercise settings across out- and in-patient samples with mild, moderate or severe depression.

An additional strength of this review is the exploration of the optimum dose-response relationship with the combination of the clinical significance and the PEDro analysis, an innovative approach in systematic reviews of exercise interventions for people with clinical depression. The particular clinical significance analysis chosen for this review used a more precise normative comparison than the previous ones (Cribbie and Arpin-Cribbie, 2009). In addition, clinical significance analysis provided clinically meaningful information regarding the improvement of depression through exercise by presenting recovery coefficients from depression. Moreover, this information provides evidence on the true antidepressant effects of exercise interventions, given that, in contrast to meta-analytic techniques, clinical significance analysis is not influenced by the potential improvement of control groups assigned to exercise control conditions. Another strength of this review is that the PEDro scale that was employed to evaluate risk of bias is more representativeand comprehensive scale than widely used scales in evaluating methodological qualities of physical therapy interventions where double blinding is impossible (Bhogal, Teasell, Foley et al., 2005). Further, the PEDro Scale shows good psychometric properties (de Morton, 2009; Macedo, Elkins, Maher et al., 2010; Maher, Sherrington, Herbert et al., 2003), and no reliability problems that other scales may present (Armijo-Olivo, Stiles, Hagen et al., 2012; Hartling, Ospina, Liang et al., 2009).

Another optimistic finding of this study deals with the fact that the number of trials and equivalence intervals in our review appeared to be comparable to a review on psychotherapy studies (Nasiakos, Cribbie and Arpin-Cribbie, 2010); psychotherapy was associated with an improvement in depression that was equivalent at the 1.5SD, 1.0SD, 0.5SD intervals in ten, five, and one studies, respectively. Although the comparison of the effectiveness of exercise with psychotherapy studies could have advanced the interpretation of our results, that was not feasible due to the lack of systematic evaluation of the methodological qualities of psychotherapy studies. Since risk of bias is linked with larger treatment effects, this evaluation is essential to control for any confounding impact of methodological inequalities on the comparative effectiveness. Psychotherapy trials face similar design issues as exercise trials (Seligman, 1995), therefore, research comparing the effectiveness and methodological qualities of exercise and psychotherapy trials is feasible.

The methodological flaws and the small number of the eligible clinical trials do not allow definite conclusions about the optimum dose-response relationship between exercise and clinical depression. Also, the representativeness of the normative data of depression used in this study to identify the clinical significance of the antidepressant effects of exercise needs to be treated with caution because of cultural and linguistic differences in comparison to a (small)-number of trial data of depression.

Conclusions

Supporting the causal interpretation of the antidepressant impact of exercise, the most effective dose-response relationship identified in this review is in line with the current guidelines for the treatment of depression through exercise on prescription and with a number of suggestions of meta-analytic reviews with sub-analyses on clinically depressed samples (Cooney, Dwan, Greig et al., 2013; Craft and Landers, 1998; Rethorst, Wipfli and Landers, 2009). The optimum dose-response relationship cannot be defined due to insufficient evidence, rather than lack of evidence. For this purpose, more RCTs with robust designs addressing the current methodological flaws seem to be essential.

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

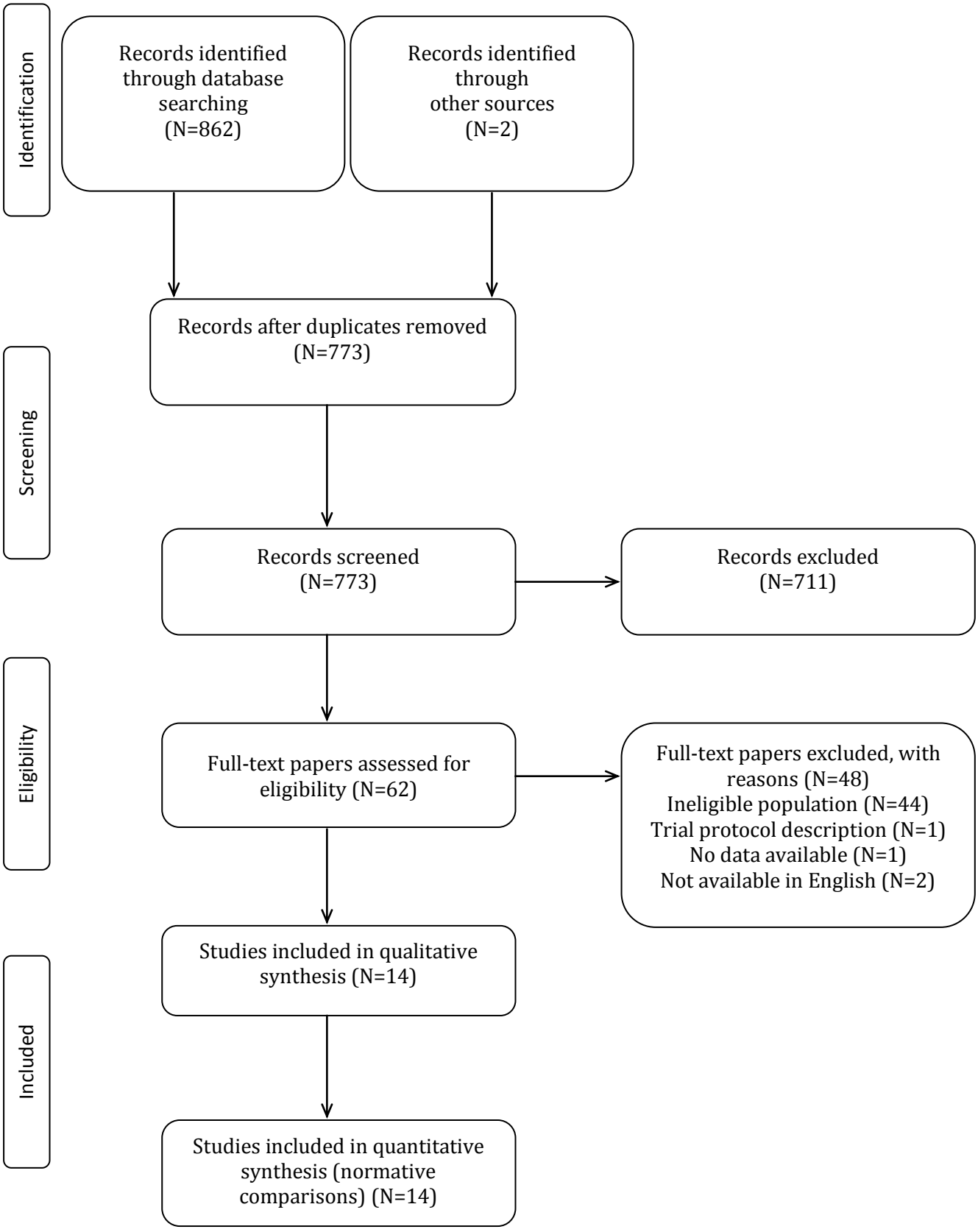


Table 1. Descriptive presentation of the reviewed trials

Trials	Interventions	N/ ♀ %	age m/sd (yrs)	attendance drop-outs %	strength vo_2max	concurrent psychiatric therapies %	depression primary outcome pre/post	post-depression equivalence interval	PEDro consensus score
Krogh et al., 2009	Outpatients, 90min/2times/week/16weeks, in groups of 3-10, supervised by physiotherapists. Location: University Hospital.								
	A. Aerobic Training Cycling, running stepping, rowing, step bench, jump rope, sliding movements on carpets abdominal, trampoline, and Ski-fitter for 2min at 70%MHR, and 2min rest. Intensity was increased to 3min at 89%MHR with 1min rest in the last 8 sessions.	55/ 81.8	41.9/ 8.7	56.2 14.5	$A^{\S}>C$ $A^{\S}>C$	70.9^{A} 43.6^{P}	HAMD-17 moderate/ improved to mild§	none	
	B. Strength Training 12 Reps X 2-3 sets on leg-chest press, leg extension, lower back, abdominals, &vertical traction at 50% of 1 Rep Max, gradually increased to 8-10 Reps at 75% of 1 Rep Maxper exercise.	55/ 78.2	38.1/ 9.0	50.6 12.7	$B^{\S}>C$ ---	67.3^{A} 50.9^{P}	moderate/ improved to mild §	none	6
	C. Relaxation Training (control group) (lower baseline depression) 20-30min relaxation exercises on a mattress, Bobath Balls or Ball Stick Ballback massage, 10-20min balance exercises, 20-30minof floor relaxation exercises alternating muscle contraction/relaxation. No cardiovascular stimulation, no ≥12 score on the Borg Scale.	55/ 61.8	36.7/ 8.7	32.8 23.6	--- ---	69.1^{A} 45.5^{P}	mild/ improved §	none	
	main inclusion criteria: referred with depression, exercising <1 times/week, no sickness leave for<24 months, no suicide risk								
Mutrie, 1986	outpatients	33/20	42.1/13.4		ame/vo_2max				
	A. Aerobic exercise Minimum of 20min/week/4weeks of outdoor or home-based individual unsupervised exercise at 60-85% MHR. A significant other could join in at the patient's preference. Individual fitness consultation for 20-30min before the program, then every 2weeks.	11/ ---	45.7/ ---	--- 18	not improved	---	BDI moderate/ improved to minimal§,†	 1.5SD 0.5SD	
	B. Stretching & strengthening exercises (control group) Individual stretching/strengthening exercises for 4 weeks at < 60% MHR. Individual fitness consultation for 20-30min before the program and then every two weeks.	11/ ---	38.9/ ---	--- 27.2	not improved	---	moderate/ unimproved	none	4
	C. No treatment for 4 weeks (control group) Awaiting an appointment with the fitness consultant.	11/ ---	41.1/ ---	--- 36.3	not improved	---	moderate/ unimproved	none	
	main inclusion criteria: >16 to <40 on BDI, no exercising, no mood improving/fitness influencing drugs								

cont..

Trials	Interventions	N/ ♀ %	age m/sd (yrs)	attendance drop-outs %	strength vo_2max	concurrent psychiatric therapies %	depression primary outcome pre/post	post-depression equivalence interval	PEDro consensus score
Mota-Pereira et al., 2011	outpatients								
	A. Aerobic Exercise (more depressed on the HAMD-17)	22/	48.6/	---	---	100[A]	HAMD-17		
	Walking 30-45min/5times/week/12weeks; individual/supervised weekly session by a sport scientist at hospital gymnasium on a treadmill, 5.0km/h/0˚ grade equal to 3.7-4 metabolic equivalents (moderate intensity). Home-based walking 4times/week, intensity prescription via accelerometers (>1952 counts) or perceived exertion (e.g., no shortness of breath). Compliance support: reminders, staff emphasized the exercise benefits,consulted family memberson social support for exercise.	57.9	2.3	14	---		severe/ improved to mild[§,†]	none	6
	B. Usual pharmacotherapy (control group)	11/	45.3/	---	---	---	mild/unimproved	none	
	Non-sedating antidepressants	80	3.1	9	---				
	main inclusion criteria: diagnosis of major depression, treatment resistance after 9-15 months of combined pharmacotherapy, no regular exercising, no psychotherapeutic treatment								
Bosscher, 1993	inpatients, mean age 34, age range 18-52, supervised exercising								
	A. Aerobic Exercise	12/	35.8/	87.5	---		SDS		
	Running 70-85%MHR 45min/3times/week/8weeks. 10min warm up (stretching), 5min cool-down (walking/stretching). Session 1-3 individual: teaching change from running to walking, correct breathing, no pain/discomfort/competitive running. Session4-24: in groups of 2-4. Location: psychiatric hospital tranquil grounds.	44	11.1	25	---	Groups attended identical care (not defined)	mild/ improved to normal[†,§]	1.5SD	4
	B. Low intensity exercises & relaxation/breathing (control group)	12/	34.7/	83.3	---		mild/		
	Low intensity training 40min/2times/week/8weeks on apparatus, volleyball soccer or trampoline with 10min warm up self-selected racket ball or soccer. Relaxation/breathing 45min/week/8weeks. Psychiatric gym. In groups of 6-12.	55	12.5	25	---		unimproved	none	
	main inclusion criteria: diagnosis of major depression, no tricyclic antidepressants,score of >40 on SDS								
de la Cerda et al., 2011	outpatients								
	A. Aerobic Exercise	41/	33.1/	---	---	100[A]	BDI-II		
	Group/supervised low impact gymnastics, walking, fun dance to increase heart rate/lung function 45-60min/3times/week/8weeks. Warm-up/cool-down. Location: Indoors (gym) and outdoors (park)	100	5.4	5	---		moderate/ improved to minimal[§,†]	1.5SD 1.0SD 0.5SD	5
	B. Pharmacotherapy (control group)	41/	31.7/	---	---	---	moderate/	1.5SD	
	All patients on antidepressants (SSRI agent Fluoxetine, 20mg).	100	6.8	0	---		improved to mild[§]	1.0SD	
	main inclusion criteria: >10 score on the BDI and >2 score of depressive symptoms on ICD-10								

cont..

Trials	Interventions	N/ ♀ %	age m/sd (yrs)	attendance drop-outs %	strength vo_2max	concurrent psychiatric therapies %	depression primary outcome pre/post	post-depression equivalence interval	PEDro consensus score
Veale et al., 1992a	outpatients, mean age 35.5, 3times/week/12weeks								
	A. Aerobic Exercise	48/	---	---	---	45[A]	CIS		
	Group/supervised running in a public park just outside hospital. Warm-up and stretching before running.	---	---	25	A[§]	100[P]	moderate-severe/ improved [§,†]	none[^]	4
	B. Treatment as usual (control group)	35/	---	---	---	34[A]	moderate-severe/		
	Supportive psychotherapy.	---	---	17.2	B		improved[§]	none[^]	
Veale et al., 1992b	A. Aerobic Exercise	63/	---	---	---	41.2[A,†]	moderate-severe /		
	Group/supervised running in a public park just outside a hospital. Warm-up and stretching before running.	87	---	26.9	---	100 [P]	improved[§]	none[^]	4
	B. Low intensity exercise (control group)	26/	---	---	---	11.5[A]	moderate-severe/		
	Group/supervised exercises of relaxation, stretching & yoga.	---	---	15.8	---	100[P]	improved[§]	1.5SD[^]	
	main inclusion criteria: >17 total weighted score&>2 depression severity score on the CIS								
Schuch et al., 2011	inpatients								
	A. Aerobic Exercise	15/ -	42.8/	---	---	100[A]	HAMD-17		
	Self-selected type of exercise (stationary bicycle, treadmill, or elliptic) and intensity 3times/week for 3 weeks, 16kcal/kg/week should be completed. Individual/supervised at hospital.	--	12.4	0	---	6[ECT]	severe/ improved tonormal[§,†]	1.5SD	
	B. Medication and/or ECT (control group)	11/	42.5/	---	---	---	severe/ improved to mild[§]	none	8
Con	All patients were prescribed antidepressants, 27% of the patients on electroconvulsive therapy. Duration 23.8 days.	---	13.5	0	---	---			
	main inclusion criteria: diagnosis of major depression, a score of ≥25 on HAMD-17, no exercising								
Schuch et al., 2015	inpatients								
	A. Aerobic Exercise	25/	38.8/	---	---	80[A]	HAMD-17		
	Self-selected type of exercise (stationary bicycle, treadmill, or stepper) and intensity3times/week for 3weeks provided that 16kcal/kg/week are completed. Individual/supervised at hospital.	72	11.5	8	---	8[ECT]	severe/ improved to normal[§,†]	none	
	B. Medication and/or ECT (control group)	25/	41.7/	---	---	---	severe/		8
	Medication therapy. 8% of the patients on ECT. Duration 23 day.	76	10.4	6	---	---	improved to mild[§]	none	
	main inclusion criteria: diagnosis of major depression, a score of ≥25on HAMD-17								

cont..

Trials	Interventions	N/ ♀ %	age m/sd (yrs)	attendance drop-outs %	strength vo_2max	concurrent psychiatric therapies %	depression primary outcome pre/post	post-depression equivalence interval	PEDro consensus Score
Krogh et al., 2012	group exercise 45min/3sessions/week/12weeks supervised by a physiotherapist. Outpatients, location undefined								
	A. Aerobic Exercise Moderate intensityon stationary cycle ergometer. 10min warm-up and 5min cool-down. Exercising at ≥65, ≥70, and ≥80%of Vo_2max in months 1, 2, 3, respectively.	56/ 71.4	39.7/ 11.3	37.5 16.1	--- A§ †	---	HAMD-17 moderate/ improved to mild§	none	7
	B. Stretching (control group) Warm up: cycling on a stationary cycle ergometer for 10min at low intensity. 20min stretching. Throwing/catching balls at low intensity for 15min.	59/ 62.7	43.4/ 11.2	34.7 10.2	--- B	---	moderate/ improved to mild§	none	
	main inclusion criteria: diagnosis of major depression, exercising ≤ 1 hour/week, no suicide risk, no psychotherapeutic treatment, no antidepressants in the last 2 months prior to the study								
Martinsen et al., 1985	inpatients, mean age 40, age range 17-60, group/supervised 60min/3times/week/9weeks								
	A. Aerobic Exercise Outdoor jogging & walking at 50-70% vo_2max supplemented by bicycling and/or swimming sessions at the patient's preference.	28/ ---	--- ---	--- 14.2	--- A§ †	32^{A} $100^{P,OT}$	BDI moderate/improved to mild§†	1.5SD 1.0SD	
	2.Occupational Therapy (control group) All patients on occupation therapy.	21/ ---	--- ---	--- 10.5	--- B	66^{A} 100^{P}	moderate/ improved§	none	5
	main inclusion criteria: diagnosis of major depression								
Reuter, 1980	outpatients, age range 18-30	22/82							
	A. Aerobic Exercise Individual/supervised running for at least 20min/3times/week/10 weeks. Non-competitive, pace allowed talking, no distance/speed level criteria. Location: indoor sport track in public sport facilities.	11/ ---	--- ---	--- 18	--- ---	$100^{C,†}$	BDI moderate/ improved tominimal§,†	1.5SD 1.0SD	4
	B. Counselling Therapy (control group) Group & individual counselling for at least 30min/week/12weeks. Also, on waiting list for joining in the aerobic exercise program.	11/ ---	--- ---	--- 18	--- ---	---	moderate/unimproved§	none	
	main inclusion criteria: a score of >15 on BDI								

cont..

Trials	Interventions	N/ ♀ %	age m/sd (yrs)	attendance drop-outs %	strength vo_2max	concurrent psychiatric therapies %	depression primary outcome pre/post	post-depression equivalence interval	PEDro consensus Score
Bosscher et al., 1997	Outpatients, mean age 41.6								
	A. Aerobic exercise A weekly session/12weeks, individual/supervised (co-running) interval running with walking/stretching breaks and input for enjoyment/preferring little effort. Gradually from light jogging to intensive running. Week 5-12:emphasis on physiological aspects. Extraunsupervised sessions, content/ number undefined. Location: public park at walking distance from clinic.	7/ ---	--- ---	--- 0	--- A§	~20A	HAMD-17 severe/ improved to normal§,†	1.5SD	5
	B. Treatment as usual (control group) Supportive psychotherapy one time per week, biweekly or thrice per week (not clear) as part of treatment programme.	7/ ---	--- ---	--- 0	--- B	~40A	severe/ unimproved	none	
	main inclusion criteria: diagnosis of major depression, a score of ≥16 on HAMD-17&on BDI								
Pilu et al., 2007	inpatients, age range 40-60 years								
	A. Aerobic Exercise Group training for 60min/2times/week/32weeks. 5min warm up, 50min on a self-selected cardio-fitness machine, change every 4min(20 options), 5min cooling down/stretching. Supervisor qualified in sport, psychology and sport psychopathology.	100/ 10	--- ---	--- 0	--- ---	100A	HAMD-17 severe/ improved to normal-mild§, †	none	6
	B. Pharmacotherapy (control group) 70% & 10% of the patients on SSRIs and SNRIs, respectively, 5% of the patients on SSRI +SNRI+Tricyclic antidepressants.	100/ 20	--- ---	--- 0	--- ---	---	severe/ unimproved	none	
	main inclusion criteria: diagnosis of major depression, female, 2month persistence of score of >13 on HAMD-17 despite medication								

A: antidepressants, AME: abdominal muscle endurance, BDI: Beck Depression Inventory, BRMS: Bech-Rafaelsen Melancholy Scale, CIS: Clinical Interview Schedule, C: counselling, ECT: electroconvulsive therapy, HAMD-17: Hamilton Rating Scale Depression, Max: maximum, MHR: maximum heart rate, OT: occupational therapy, P: psychotherapy, Rep: repetition, SCL-90: Symptom Checklist-90, SD: standard deviation, SDS: Self-rating Depression Scale, SNRI: serotonin-norepinephrine reuptake inhibitor, SSRI: selective serotonin reuptake inhibitor, Vo_2max: maximum aerobic capacity, §: Statistically significant difference within group, †: Statistically significant difference between groups, ^: Equivalence on the CIS-R.

Table 2. PEDro Consensus Scores of randomized controlled trials

PEDro Criteria	Random Allocation	Allocation Concealment	Balance Baseline	Blinding patient/therapist/assessor	Drop-outs (<15%)	Intention to treat	Statistical comparison between groups	Point/variability measures	PEDro Total
RCTs									
Schuch et al., 2015	1	1	1	0/0/1	1	1	1	1	8
Schuch et al., 2011	1	1	1	0/0/1	1	1	1	1	8
Krogh et al., 2012	1	1	1	0/0/1	0	1	1	1	7
Krogh et al., 2009	1	1	0	0/0/1	0	1	1	1	6
Pilu et al., 2007	1	0	1	0/0/0	1	1	1	1	6
Mota-Pereira et al., 2011	1	1	0	0/0/1	1	0	1	1	6
Martinsen et al., 1985	1	0	1	0/0/0	1	1	1	0	5
Bosscher et al., 1997*	0	0	1	0/0/0	1	1	1	1	5
delaCerda et al., 2011*	0	0	1	0/0/0	1	1	1	1	5
Veale et al., 1992a	1	0	1	0/0/0	0	0	1	1	4
Veale et al., 1992b	1	0	1	0/0/0	0	0	1	1	4
Bosscher, 1993	1	0	1	0/0/0	0	0	1	1	4
Mutrie, 1986	1	0	1	0/0/0	0	0	1	1	4
Rueter, 1980	1	0	1	0/0/0	0	0	1	1	4

RCTs: randomized controlled trials, *control trials

Table 3. Normative comparisons for aerobic exercise groups

Trials	Primary Outcome Measures							Δ Pre-Post p<.05	PEDro Consensus Score	Normative Equivalence of depression at post-treatment			Normative References
	pre-treatment			post-treatment			tools			level of equivalence			
	M	SD	N	M	SD	N				±0.5SD	±1.0SD	±1.5SD	
Schuch et al., 2011	25.6	2.6	15	5.9	4.5	15	HAMD-17	YES	8			E	Zimmerman et al., 2004a
Martinsen et al., 1985	26	7.4	28	13	7.4	24	BDI	YES	5		E	E	Aasen, 2001
de la Cerda et al., 2011	26.3	2.5	41	8.6	5.4	41	BDI	YES	5	E	E	E	Sanz et al., 2003
Bosscher et al., 1997	22.6	7.2	7	4.5	2.9	7	HAMD-17	YES	5			E	Zimmerman et al., 2004a
Bosscher, 1993	53.7	5.5	12	41.2	10.5	9	SDS	YES	4			E	Campo-Arias et al., 2006
Rueter, 1980	23	7.6	11	5.1	4.75	9	BDI	YES	4		E	E	Seggar et al., 2002
Mutrie, 1986	22.4	6.8	11	9.5	4.3	9	BDI	YES	4		E	E	Seggar et al., 2002

M: mean, SD: standard deviation, N: number, HAMD-17: Hamilton Rating Scale Depression, BDI: Beck Depression Inventory, SDS: Self-rating Depression Scale, E: equivalent

Chapter 4. Study 3

Aerobic exercise in routine practice. A systematic review and meta-analysis

Abstract

This review examined the antidepressant effect of aerobic exercise as an add-on intervention.Eight e-databases were searched for randomized controlled clinical trials comparing aerobic exercise to conventional antidepressant treatments in clinically depressed patients (18-65 years) referred by health services. A random effects model using Hedges'g pooled post-depression scores. The I^2 and Cochrane Q measured heterogeneity. Funnel plot visual inspection, the Begg-Mazumbar Kendall's tau and Egger tests investigated for publication bias. Coding included intervention/patient characteristics (duration, frequency, intensity, symptom severity, outpatients, inpatients) and risk of bias for individual trials.Across 12 eligible RCTs, moderate intensity aerobic exercise showed a significantly large overall antidepressant effect-size (ES) with low and non-statistically significant heterogeneity (ES=-0.83, 95% CI=-1.02, -0.62, I^2=20.89%, PQ=0.226). Mazumbar Kendall's tau and Egger tests showed no publication bias. Subgroup analyses revealed large or moderate to large ESs for exercise with low or moderate levels of heterogeneity (I^2= ≤40%; Cochrane Q p>0.05). Moderate intensity aerobic exercise of 3times/week led depressed patients to an improvement in depression. Similar findings were found for both short- (1-4weeks) and longer-term (8-12weeks) aerobic exercise, across indoor or outdoor settings and in both outpatient and inpatient samples regardless age rage or symptom severity. Also, trials with lower risk of bias showed comparable effects. Our findings are congruent with a previous meta-analytic review with clinically depressed samples (Rethorst, Wipfli and Landers, 2009).Aerobic exercise is considered an effective antidepressant intervention.

Introduction

Physical exercise has repeatedly been associated with an improvement in depression in depressed adults(Craft and Landers, 1998; Rethorst, Wipfli and Landers, 2009; Robertson, Robertson, Jepson et al., 2012; Schuch, Vancampfort, Richards et al., 2016; Silveira, Moraes, Oliveira et al., 2013; Stanton and Reaburn, 2014). Nevertheless, there is no consensus on whether this association is causal due to claims for limited evidence resulting from methodologically flawed trials and a small number of participants who may often be unrepresentative to the population of interest (Cooney, Dwan and Mead, 2014; Cooney, Dwan, Greig et al., 2013; Lawlor and Hopker, 2001). Researchers, however, have raised serious doubts about the above inconclusive views on the anti-depressiveness of exercise (Blumenthal and Ong, 2009; Ekkekakis, 2015; Spedding, 2015). In light of the current synthesis of literature, however, no meta-analysis has exclusively reviewed exercise trials with clinically depressed adult referred from health services to compare aerobic exercise to routine practice treatment conditions, nor evaluated the methodological qualities of such trials through a standardized process based on tools designed for physical therapy interventions.

Therefore, the aim of this meta-analysis is to review the antidepressant effects of physical exercise in clinically depressed adult patients.

Methodology

This review was conducted in accordance to the Preferred Items for Systematic Reviews and Meta-Analyses (PRISMA) statement that ensures quality through a standard list of 27 items(Moher, Liberati and Tetzlaff, 2009). Eligibility criteria in terms of study characteristics were based on the PICOS criteria; Participants, Intervention, Comparison, Outcome and Study design (PICOS). Participants; 18-65 years old, recruited via health services with a referral or with a previous diagnosis of major depression as a primary outcome without psychotic features and not as a result of a mental or medical disorder/condition. Intervention; exercise interventions as defined by the American College of Sports Medicine. Comparison; comparison of exercise interventions to other treatments, or waiting list. Outcome; depression as the primary outcome measure. Study design; studies with a design of a randomized controlled trial (RCT). Regarding eligibility criteria in terms of report characteristics, the search covered the period from 1980 to present and was conducted in February 2017 for RCTs written in English.

The following electronic databases were searched: Mediline, PsyINFO, SPORTDiscus, Academic Search Complete, Education Resource Information Centre, Embase, and Web of

Science, Trials Register of Promoting Health Interventions (TRoPHI; EPPI Centre) http://eppi.ioe.ac.uk/webdatabases4/Search.aspx, ClinicalTrials.Gov https://clinicaltrials.gov/ct2/search/advanced and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) http://www.who.int/ictrp/search/en/http://apps.who.int/trialsearch/. The Proquest Dissertations and Theses database was searched for unpublished studies in order to avoid publication bias. Search terms were "clinical*" "depress*", "major", "disorder", "diagnos*", "refer*", "patient", or "adult" AND "exercise", "aerobic", "strength", "cardio", "training", "weight", "resistance", "jog*", or "run*". Hand-searching was conducted to screen references lists. RCTs were initially screened through titles and abstracts. Full text versions were obtained subject to positive initial screening.

Data were extracted and checked for accuracy and for duplicates onto prepared forms based on the PICOS criteria. Most authors of eligible trials were contacted to provide additional information. To control for risk of bias, methodological quality of all eligible RCTs were assessed with the Physiotherapy Evidence-based Database scale (PEDro). This scale is a well-established comprehensive measure of methodological quality in the physical therapy literature (Bhogal, Teasell, Foley et al., 2005), it shows good psychometric properties (de Morton, 2009; Macedo, Elkins, Maher et al., 2010; Maher, Sherrington, Herbert et al., 2003) and it is increasingly used in various research areas (Brown, Huedo-Medina, Pescatello et al., 2011; Knols, de Bruin, Shirato et al., 2010; Pan, Wang, Xie et al., 2014; Pinto, Maher, Ferreira et al., 2012). Criteria 2-11 assess internal validity that lead to a maximum score of 10 by allocating two points for between-groups comparisons and point estimates/variability measures, three points for blinding patients/therapists/assessors, two points for random/concealment allocation, and three points for baseline balance, intention-to-treat, and <15% drop-out rates. The maximum score in our study was set to be 8, deducting the two points for blinding, as it is difficult, if not impossible, to blind patients/therapists in exercise trials for depression. An independent researcher assessed the methodological quality of each trial, and sought consensus with the author's evaluations on the relevant evaluations. Cohen's Kappa statistic was computed, and interpreted based on the Landis and Koch (Landis and Koch, 1977) reference to estimating the inter-rater agreement (0.81-1.0, 0.61-0.80, 0.41-0.60, 0.21-0.40, 0.0-0.20 and <0, as nearly perfect, substantial, moderate, fair, slight and poor, respectively).

Coding included methodological qualities (PEDro score ≤6 OR score ≥7), participants' characteristics including gender (males, females OR more [>50%] males or females),

hospitalized or non-hospitalized (outpatients OR inpatients), age (younger [18-39] OR mature adults [40-65]), intervention characteristics including duration (≤1month, ≤3 months OR >3 months), frequency (≤3 days/week, 3 days/week OR >3 days/week), intensity (lower, moderate or vigorous), setting (outdoors OR indoors), and social format (individually OR in groups).

The software (version-2) Comprehensive Meta-Analysis was used to calculate effect sizes. A random effects model using the Hedges' g criterion measured standardized mean differences in depression between exercise and control groups (Borenstein, Hedges, Higgins et al., 2010). The selection of a random effects model lies upon the assumption that there is a sampling error (within-study error) and between-study variance. The Hedges' g criterion prevents overestimation of an effect size when the retrieved studies are less than 20.

Statistical heterogeneity was evaluated with the Cochran Q and I^2 statistics for each trial (Higgins, Thompson, Deeks et al., 2003) taking into consideration that I^2 values up to 40% are unlikely to be important (Higgins and Green, 2011). Publication bias was assessed by means of visual inspection of the funnel plots and the Begg-Mazumbar Kendall's tau (Begg and Mazumdar, 1994) and Egger bias test (Egger, Smith, Schneider et al., 1997). Also, the trim and fill statistical procedure was computed for the main composite analysis (Duval and Tweedie, 2000). This procedure adds or removes studies to balance an asymmetrical funnel plot and re-calculates the effect size accordingly. In this manner, an unbiased estimate of the effect size is provided. Also, the fail-safe criterion (Rosenthal, 1979) was employed to calculate the number of studies needed to nullify significant effects (e.g., >0.05). A fail-safe number of five times the number of reviewed RCTs plus 10 (5K+10) is seen as the standard cutoff score for evaluating the results as robust(Rosenthal, 1979). Finally, sensitivity analyses involved consideration that less than 5 trials as estimates of effect size may reveal imprecise results (Borenstein, Hedges, Higgins et al., 2009).

Results

The literature search is illustrated in the flow chart (Figure 1). Twelve RCTs (George, Chandran. Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Oertel-Knöchel, Mehler, Thiel et al., 2014; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015; Veale, Le Fevre, Pantelis et al., 1992a) were eligible for inclusion.

Participants

Outpatients or inpatients: Participants were outpatients in six RCTs (George, Chandran. Mohan and Sandesh, 2012; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016; Veale, Le Fevre, Pantelis et al., 1992a) and inpatients in the remaining six RCTs (Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Oertel-Knöchel, Mehler, Thiel et al., 2014; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015).

Symptom severity: Participants were diagnosed with mild-moderate or moderate depression in five RCTs (George, Chandran. Mohan and Sandesh, 2012; Martinsen, Medhus and Sandvik, 1985; Oertel-Knöchel, Mehler, Thiel et al., 2014; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016) and with moderate-severe or severe depression in seven RCTs (Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015; Veale, Le Fevre, Pantelis et al., 1992a) . In two of the above RCTs, patients had severe and treatment resistant depression (Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007).

Younger or mature adults: Five and seven RCTs, respectively, recruited depressed patients with an age range of 18-39 (George, Chandran. Mohan and Sandesh, 2012; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016; Salehi, Hosseini, Haghighi et al., 2016; Veale, Le Fevre, Pantelis et al., 1992a) or 40-65 years old (Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Oertel-Knöchel, Mehler, Thiel et al., 2014; Pilu, Sorba, Hardoy et al., 2007; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015).

Males or females: In four RCTs, samples comprised mainly male participants (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Sadeghi, Ahmadi, Ahmadi et al., 2016; Salehi, Hosseini, Haghighi et al., 2016). In six RCTs, samples comprised mainly female participants(Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Oertel-Knöchel, Mehler, Thiel et al., 2014; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015). In two RCTs, males and females represented 50% of the sample (Oertel-Knöchel, Mehler, Thiel et al., 2014; Veale, Le Fevre, Pantelis et al., 1992a).

Intervention characteristics

Weekly frequency: Aerobic exercise was employed 3 times per week in eight RCTs (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Martinsen, Medhus and Sandvik, 1985; Oertel-Knöchel, Mehler, Thiel et al., 2014; Rueter, 1980; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015; Veale, Le Fevre, Pantelis et al., 1992a), 2 times per week in one RCT (Pilu, Sorba, Hardoy et al., 2007), 5 times per week in one RCT (Mota-Pereira, Silverio, Carvalho et al., 2011), and one a daily basis in one RCT (Legrand and Neff, 2016). Finally, one RCT did not provide any information about the weekly frequency (Sadeghi, Ahmadi, Ahmadi et al., 2016).

Session duration: Nine RCTs provided information about session duration (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Oertel-Knöchel, Mehler, Thiel et al., 2014; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015), time of sessions ranged from 20min to 60min, with an average of 45min. In three (Kerling, Tegtbur, Gützlaff et al., 2015; Martinsen, Medhus and Sandvik, 1985; Sadeghi, Ahmadi, Ahmadi et al., 2016) and five RCTs (George, Chandran. VV.Mohan and Sandesh, 2012; Legrand and Neff, 2016; Oertel-Knöchel, Mehler, Thiel et al., 2014; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) session duration lasted between >45min to 60min, and 30min to 45min, respectively.

Total duration: Aerobic exercise of up to six weeks was found in five RCTs (Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Oertel-Knöchel, Mehler, Thiel et al., 2014; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) and between 8 to 12 weeks in six RCTs (George, Chandran. VV.Mohan and Sandesh, 2012; Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016; Veale, Le Fevre, Pantelis et al., 1992a). One RCT used a 32week long aerobic exercise programme (Pilu, Sorba, Hardoy et al., 2007).

Intensity: Ten RCTs employed moderate intensity exercise on average. Prescription was based on Vo2max (Martinsen, Medhus and Sandvik, 1985; Salehi, Hosseini, Haghighi et al., 2016), maximum heart rate reserve (George, Chandran. VV.Mohan and Sandesh, 2012; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015), maximum heart rate (Legrand and Neff, 2016; Oertel-Knöchel, Mehler, Thiel et al., 2014; Sadeghi, Ahmadi, Ahmadi et al., 2016), RPE (Kerling, Tegtbur, Gützlaff et al., 2015), the “walking and talking” approach by

instructing patients to be able to talk when exercising (Rueter, 1980) or treadmill speed (5km/h) with advice to avoid shortness of breath (Mota-Pereira, Silverio, Carvalho et al., 2011). Two RCTs did not report the intensity exercise (Pilu, Sorba, Hardoy et al., 2007; Veale, Le Fevre, Pantelis et al., 1992a).

Aerobic exercise modality: Equipment-free or equipment-based: Five RCTs used equipment-free aerobic exercise programmes including walking and/or running (Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Rueter, 1980; Veale, Le Fevre, Pantelis et al., 1992a) or running in place combined with various bodily exercises (Sadeghi, Ahmadi, Ahmadi et al., 2016). Seven RCTs used equipment-based programmes (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Oertel-Knöchel, Mehler, Thiel et al., 2014; Pilu, Sorba, Hardoy et al., 2007; Sadeghi, Ahmadi, Ahmadi et al., 2016; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015). In four of the latter RCTs, patients could conduct preference-based training by selecting equipment out of a range of available options (Kerling, Tegtbur, Gützlaff et al., 2015; Martinsen, Medhus and Sandvik, 1985; Pilu, Sorba, Hardoy et al., 2007; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) and regulating the intensity provided that specific metabolic equivalents (16kcal/kg/week) would be completed per session (Schuch, Vasconcelos-Moreno, Borowsky et al., 2015). One RCT used an aerobic exercise programme comprising a treadmill-based session and home-based sessions without clarifying if they were equipment-based or equipment-free (Mota-Pereira, Silverio, Carvalho et al., 2011).

Group or individually: Six RCTs employed group-based (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Martinsen, Medhus and Sandvik, 1985; Oertel-Knöchel, Mehler, Thiel et al., 2014; Pilu, Sorba, Hardoy et al., 2007; Veale, Le Fevre, Pantelis et al., 1992a) and five RCTs individual-based (Legrand and Neff, 2016; Mota-Pereira, Silverio, Carvalho et al., 2011; Rueter, 1980; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) aerobic exercise protocols. One RCT did not provide relevant information (Sadeghi, Ahmadi, Ahmadi et al., 2016).

Dropouts: In six and three RCTs drop-out rates were <15% (Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) and ≥15%(Oertel-Knöchel, Mehler, Thiel et al., 2014; Rueter, 1980; Veale, Le Fevre, Pantelis et al., 1992a), respectively. The remaining tree

RCTs did not report relevant information (George, Chandran. VV.Mohan and Sandesh, 2012; Pilu, Sorba, Hardoy et al., 2007; Sadeghi, Ahmadi, Ahmadi et al., 2016).

Indoor settings: Indoor- and outdoor-based aerobic exercise was adopted by sevenXX(Kerling, Tegtbur, Gützlaff et al., 2015; Mota-Pereira, Silverio, Carvalho et al., 2011; Oertel-Knöchel, Mehler, Thiel et al., 2014; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) and three (Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Veale, Le Fevre, Pantelis et al., 1992a) RCTs, respectively. Two RCTs did not provide relevant information (George, Chandran. VV.Mohan and Sandesh, 2012; Sadeghi, Ahmadi, Ahmadi et al., 2016)

Hospital or non-hospital settings: Four RCTs were carried out inside a hospital setting (Kerling, Tegtbur, Gützlaff et al., 2015; Oertel-Knöchel, Mehler, Thiel et al., 2014; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) and five outside a hospital setting (Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Veale, Le Fevre, Pantelis et al., 1992a). One RCT adopted mixed settings (hospital and home) (Mota-Pereira, Silverio, Carvalho et al., 2011), and two RCTs did not present relevant information (George, Chandran. VV.Mohan and Sandesh, 2012; Sadeghi, Ahmadi, Ahmadi et al., 2016).

Comparisons

Aerobic exercise vs. all control groups conditions: Aerobic exercise was compared to antidepressants in four RCTs (George, Chandran. VV.Mohan and Sandesh, 2012; Legrand and Neff, 2016; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007), treatment as usual in three RCTs (Kerling, Tegtbur, Gützlaff et al., 2015; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015; Veale, Le Fevre, Pantelis et al., 1992a), and in three RCTs, respectively, to occupational (Martinsen, Medhus and Sandvik, 1985), counselling (Rueter, 1980) or cognitive (Sadeghi, Ahmadi, Ahmadi et al., 2016) therapy. In the latter study the second comparator involved an unsupervised and self-administrative group discussion among the patients themselves. One trial was a three-arm RCT comparing i) aerobic exercise to electroconvulsive therapy (ECT) and ii) aerobic exercise combined with ECT to ECT (Salehi, Hosseini, Haghighi et al., 2016). Another RCT compared aerobic exercise to waiting list (Oertel-Knöchel, Mehler, Thiel et al., 2014). In all but one RCT (Sadeghi, Ahmadi, Ahmadi et al., 2016) aerobic exercise was employed as an add-on intervention.

Outcome measures: Seven trials (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015; Veale, Le Fevre, Pantelis et al., 1992a) and five trials (Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Oertel-Knöchel, Mehler, Thiel et al., 2014; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016) used clinician-rated and self-rated primary outcomes of depression, respectively (Table 2). The clinician-rated outcomes included the Clinical Interview Scale (Goldberg, Cooper, Eastwood et al., 1970) in one trial (Veale, Le Fevre, Pantelis et al., 1992a), the Montgomery-Åsberg Depression Scale (Montgomery and Asberg, 1979) in one trial (Kerling, Tegtbur, Gützlaff et al., 2015) and the Hamilton rating scale for Depression (Hamilton, 1960) in five trials (George, Chandran. VV.Mohan and Sandesh, 2012; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015). The self-rated outcomes included the Beck Depression Inventory (Beck, Ward, Mendelson et al., 1961) in two trials (Martinsen, Medhus and Sandvik, 1985; Rueter, 1980) and the Beck Depression Inventory-II (Beck, Steer and Brown, 1996) in three trials(Legrand and Neff, 2016; Oertel-Knöchel, Mehler, Thiel et al., 2014; Sadeghi, Ahmadi, Ahmadi et al., 2016).

Study Design

*Methodological qualities:*Evaluation of methodological qualities, indicated that four trials reached the top scores of 8 (Kerling, Tegtbur, Gützlaff et al., 2015; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) or 7 (Legrand and Neff, 2016; Salehi, Hosseini, Haghighi et al., 2016) on the PEDro scale, two the score of 6 (Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007), five the score of 5 (George, Chandran. VV.Mohan and Sandesh, 2012; Martinsen, Medhus and Sandvik, 1985; Oertel-Knöchel, Mehler, Thiel et al., 2014; Sadeghi, Ahmadi, Ahmadi et al., 2016; Veale, Le Fevre, Pantelis et al., 1992a), and one trial the score of 4 (Rueter, 1980) (Table 2).Cohen's Kappa statistic was 0.77, indicating a substantial inter-rater reliability on the PEDro scoring (Landis and Koch, 1977). Details are illustrated in Supplementary Material-1.

Dropouts: The intervention and the control groups did not show statistically significant differences in the number of patients who dropped out.

Details of all reviewed RCTs can be found in Supplementary Material-2.

Meta-analysis

Across twelve eligible RCTs (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Oertel-Knöchel, Mehler, Thiel et al., 2014; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015; Veale, Le Fevre, Pantelis et al., 1992a), aerobic exercise showed a statistically significant overall large antidepressant effect compared to routine practice treatment conditions with low and non-statistically significant heterogeneity (ES= -0.82, CI 95% -1.02 to -0.62 p=0.000, Q=16.435 p=0.226 I^2=20.88%). Also, the Begg-Mazundar Kendall's tau (tau -0.087 p=0.661) and Egger bias test (intercept -0.754, p=0.567) indicated no publication bias. Therefore, computation of trim and fill analysis did not appear to be essential (for the readers' information relevant results can be found in table-1, in the supplementary material). Moreover, the fail-safe algorithm indicated that 299 studies with no antidepressant effect for aerobic exercise would be required to nullify the significance of the main result. This finding indicates no publication bias given that the relevant fail-safe standard (5k+10) for this review is 100 studies. The corresponding tables of the following sensitivity analyses can be found in supplementary material (study-3).

Sensitivity analyses

Participants

Outpatients or inpatients. Among the six trials with depressed outpatients (George, Chandran. VV.Mohan and Sandesh, 2012; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016; Veale, Le Fevre, Pantelis et al., 1992a), aerobic exercise showed a significant large antidepressant impact (ES= -0.89, CI95% -1.15 to -0.63, p=0.000, Q= 6.79, p=0.340, Begg tau -0.285, p=0.367, Egger intercept -0.848, p=0.588, I^2=11.69%). A similar impact was seen in the six RCTs with depressed inpatients (ES= -0.75, CI95% -1.06 to -0.44, p=0.000, Q= 8.895, p=0.180, Begg tau -0.000, p=1.000, Egger intercept -1.355, p=0.669, I^2=32.54%) (Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Oertel-Knöchel, Mehler, Thiel et al., 2014; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015).

Symptom severity: Significantly large and moderate to large effect sizes for aerobic exercise were found across the five (George, Chandran. VV.Mohan and Sandesh, 2012;

Martinsen, Medhus and Sandvik, 1985; Oertel-Knöchel, Mehler, Thiel et al., 2014; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016) and seven (Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015; Veale, Le Fevre, Pantelis et al., 1992a) trials with patients with mild-moderate/moderate or moderate-severe/severe depression, respectively (mild-moderate/moderate: ES= -0.98, CI95% -1.31 to -0.65, p=0.000, Q= 6.906, p=0.228, Begg tau -0.066, p=0.850, Egger intercept -0.422, p=0.815, I^2=27.59%; moderate-severe/severe: ES= -0.71, CI95% -0.93 to -0.48, p=0.000, Q= 7.163, p=0.412, Begg tau -0.178, p=0.536, Egger intercept -1.918, p=0.416, I^2=2.27%).

Younger or mature adults: In the five trials with younger adult patients (18-39 years old) (George, Chandran. VV.Mohan and Sandesh, 2012; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016; Salehi, Hosseini, Haghighi et al., 2016; Veale, Le Fevre, Pantelis et al., 1992a) aerobic exercise showed a significant, large reductive effect on depression with marginally significant moderate heterogeneity (ES= -0.83, CI95% -1.17 to -0.48, p=0.000, Q= 12.707, p=0.048, Begg tau -0.095, p=0.763, Egger intercept -1.029, p=0.665, I^2=52.78%). A significant, large impact for aerobic exercise was recorded in the seven trials with mature adult patients (40-65 years old) (Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Oertel-Knöchel, Mehler, Thiel et al., 2014; Pilu, Sorba, Hardoy et al., 2007; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) (ES= -0.82, CI95% -1.09 to -0.55, p=0.000, Q= 3.728, p=0.713, Begg tau -0.000, p=1.000, Egger intercept -0.518, p=0.792, I^2=0%).

Males or Females: Data polled from four trials with samples comprising mainly male patients, (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Sadeghi, Ahmadi, Ahmadi et al., 2016; Salehi, Hosseini, Haghighi et al., 2016) revealed a significant moderate to large effect for aerobic exercise was seen (ES= -0.69, CI95% -1.02 to -0.36, p=0.000, Q= 8.952, p=0.111, Begg tau -0.00, p=1.00, Egger intercept -2.565, p=0.406, I^2=44.14%). Similarly, a significant large effect for aerobic exercise was found in the six trials with predominantly female patients (Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) (ES= -1.02, CI95% -1.32 to -0.72, p=0.000, Q= 4.866, p=0.432, Begg tau -0.266, p=0.453, Egger intercept -2.869, p=0.174, I^2=0%). Two trials had the same proportion (50%) of male and

female participants (Oertel-Knöchel, Mehler, Thiel et al., 2014; Veale, Le Fevre, Pantelis et al., 1992a).

Intervention characteristics

Weekly frequency: Aerobic exercise for 3 times/week was included in eight trials (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Martinsen, Medhus and Sandvik, 1985; Oertel-Knöchel, Mehler, Thiel et al., 2014; Rueter, 1980; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015; Veale, Le Fevre, Pantelis et al., 1992a) and showed a significant large reduction in scores of depression (ES= -0.84, CI95% -1.08 to -0.60, p=0.000, Q= 15.012, p=0.132, Begg tau -0.036, p=0.872, Egger intercept -0.819, p=0.595, I^2=33.38%).

Session duration: Across the nine RCTs with available information, the aerobic exercise sessions ranged from 20min to 60min (average time of 45min) and showed a significantly large impact on depression (ES= -0.83, CI95% -1.08 to -0.57, p=0.000, Q= 15.900, p=0.283, Begg tau -0.109, p=0.640, Egger intercept -0.730, p=0.658, I^2=37.10%)(George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Oertel-Knöchel, Mehler, Thiel et al., 2014; Rueter, 1980; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015). Of the nine RCTs, aerobic exercise for >45 to 60min was employed by three RCTs (Kerling, Tegtbur, Gützlaff et al., 2015; Martinsen, Medhus and Sandvik, 1985; Sadeghi, Ahmadi, Ahmadi et al., 2016) and revealed a large reductive effect on depression (ES= -0.74, CI95% -1.11 to -0.36, p=0.000, Q= 3.809, p=0.283, Begg tau -0.166, p=0.734, Egger intercept -2.720, p=0.595, I^2=21.23%). Aerobic exercise of 30 to 45min was seen in five RCTs (George, Chandran. VV.Mohan and Sandesh, 2012; Legrand and Neff, 2016; Oertel-Knöchel, Mehler, Thiel et al., 2014; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) (ES= -0.80, CI95% -1.11 to -0.49, p=0.000, Q= 7.360, p=0.195, Begg tau 0.266, p=0.452, Egger intercept 0.967, p=0.654, I^2=32.06%). Aerobic exercise of up to 45min was used by six RCTs (George, Chandran. VV.Mohan and Sandesh, 2012; Legrand and Neff, 2016; Oertel-Knöchel, Mehler, Thiel et al., 2014; Rueter, 1980; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) and showed a large antidepressant effect-size (ES= -0.89, CI95% -1.25 to -0.53, p=0.000, Q= 11.616, p=0.071, Begg tau 0.000, p=1.000, Egger intercept -0.820, p=0.678, I^2=48.34%).

Total programme duration: Aerobic exercise for up to six weeks was found in five RCTs (Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Oertel-Knöchel, Mehler, Thiel et al., 2014; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) and demonstrated a significant moderate to large effect on depression (ES= -0.66, CI95% -0.97 to -0.35, p=0.000, Q= 6.341, p=0.274, Begg tau -0.000, p=1.000, Egger intercept -1.530, p=0.611, I^2=21.15%). Similarly, in the four RCTs with 4week aerobic exercise programmes, a significant moderate to large antidepressant effect was recorded (ES= -0.71, CI95% -1.09 to -0.34, p=0.000, Q= 5.797, p=0.215, Begg tau -0.000, p=1.000, Egger intercept -1.185, p=0.737, I^2=30.99%) (Legrand and Neff, 2016; Oertel-Knöchel, Mehler, Thiel et al., 2014; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015). A significantly large effect was seen in the five trials where aerobic exercise was conducted for 8-12 weeks (ES= -0.92, CI95% -1.19 to -0.65, p=0.000, Q= 7.618, p=0.267, Begg tau -0.095, p= 0.763, Egger intercept -0.932, p=0.592, I^2=21.24%) (George, Chandran. VV.Mohan and Sandesh, 2012; Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016; Veale, Le Fevre, Pantelis et al., 1992a).

Exercise intensity: Ten RCTs employed moderate intensity which showed a significantly large impact on scores of depression (ES= -0.82, CI95% -1.05 to -0.58, p=0.000, Q= 16.048, p=0.139, Begg tau -0.075, p=0.731, Egger intercept -0.602, p=0.694, I^2=31.45%) (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Oertel-Knöchel, Mehler, Thiel et al., 2014; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015).

Aerobic exercise modality: Equipment-based aerobic exercise was used by six RCTs and detected a significantly large effect on depression (ES= -0.75, CI95% -1.04 to -0.47, p=0.000, Q= 8.759, p=0.188, Begg tau 0.190, p=0.548, Egger intercept 1.146, p=0.598, I^2=31.49%) (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Oertel-Knöchel, Mehler, Thiel et al., 2014; Pilu, Sorba, Hardoy et al., 2007; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015). Similar effects were found in the five RCTs with equipment-free aerobic exercise programmes (ES= -0.94, CI95% -1.28 to -0.60, p=0.000, Q= 6.964, p=0.223, Begg tau -0.400, p=0.259, Egger intercept -3.003, p=0.171, I^2=28.20%) (Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016; Veale, Le

Fevre, Pantelis et al., 1992a). Also, in the four RCTs where preference-based exercising was enforced (Kerling, Tegtbur, Gützlaff et al., 2015; Martinsen, Medhus and Sandvik, 1985; Pilu, Sorba, Hardoy et al., 2007; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015), aerobic exercise reduced depression by a significant, large effect (ES= -0.84, CI95% -1.17 to -0.51, p=0.000, Q= 3.227, p=0.358, Begg tau -0.166, p=0.734, Egger intercept -3.727, p=0.521, I^2=7.04%) .

Group- or individual-based aerobic exercise: Group-based aerobic exercise was employed by six RCTs (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Martinsen, Medhus and Sandvik, 1985; Oertel-Knöchel, Mehler, Thiel et al., 2014; Pilu, Sorba, Hardoy et al., 2007; Veale, Le Fevre, Pantelis et al., 1992a) and reduced depression by a significant, large effect (ES= -0.88, CI95% -1.12 to -0.64, p=0.000, Q= 4.298, p=0.507, Begg tau -0.000, p=1.000, Egger intercept -0.636, p=0.709, I^2=0%). Individual-based aerobic exercise was recorded in five RCTs (Legrand and Neff, 2016; Mota-Pereira, Silverio, Carvalho et al., 2011; Rueter, 1980; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015), and was linked with significantly large effects as well as with moderate heterogeneity that was marginally non-statistically significant (ES= -0.86, CI95% -1.30 to -0.43, p=0.000, Q= 10.775, p=0.056, Begg tau -0.400, p=0.259, Egger intercept -4.386, p=0.143, I^2=53.59%).

Drop-outs: The synthesis of data from the six trials with drop-out rates of <15% (Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) revealed a significant moderate to large effect size for aerobic exercise (ES= -0.75, CI95% -1.05 to -0.45, p=0.000, Q= 8.868, p=0.181, Begg tau -0.095, p=0.763, Egger intercept -2.713, p=0.503, I^2=32.34%). In the three trials (Oertel-Knöchel, Mehler, Thiel et al., 2014; Rueter, 1980; Veale, Le Fevre, Pantelis et al., 1992a) with dropout rates of ≥15%, a significantly large effect size was found (ES= -1.02, CI95% -1.75 to -0.30, p=0.000, Q= 4.605, p=0.100, Begg tau -0.666, p=0.296, Egger intercept -2.324, p=0.559, I^2=56.56%).

Indoor or outdoor settings: Seven and three RCTs, respectively, included indoor-based (Kerling, Tegtbur, Gützlaff et al., 2015; Mota-Pereira, Silverio, Carvalho et al., 2011; Oertel-Knöchel, Mehler, Thiel et al., 2014; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) and outdoor-based (Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Veale, Le Fevre, Pantelis et al., 1992a) aerobic exercise programmes which reduced depression by

significant, large effect sizes(indoors: ES= -0.77, CI95% -1.10 to -0.44, p=0.000, Q= 12.045, p=0.099, Begg tau -0.250, p=0.386, Egger intercept -3.537, p=0.130, I^2=41.88%; outdoors: ES= -0.94, CI95% -1.30 to -0.58, p=0.000, Q= 1.370, p=0.504, Begg tau -0.000, p=1.000, Egger intercept -1.946, p=0.590, I^2=0%).

Hospital or non-hospital settings: In the four trials conducted inside a hospital setting (Kerling, Tegtbur, Gützlaff et al., 2015; Oertel-Knöchel, Mehler, Thiel et al., 2014; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015), the impact of aerobic exercise on depression was moderate and significant (ES= -0.61, CI95% -0.96 to -0.27, p=0.000, Q= 5.615, p=0.230, Begg tau -0.000, p=1.000, Egger intercept -0.638, p=0.876, I^2=28.76%). Also, a significant large impact was found in the five trials conducted outside a hospital setting (Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Veale, Le Fevre, Pantelis et al., 1992a) (ES= -1.06, CI95% -1.41 to -0.72, p=0.000, Q= 4.652, p=0.325, Begg tau -0.300, p=0.462, Egger intercept -3.081, p=0.089, I^2=14.01%).

Comparisons

Comparison to routine practice treatment conditions: Across the twelve eligible trials reviewed (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Oertel-Knöchel, Mehler, Thiel et al., 2014; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015; Veale, Le Fevre, Pantelis et al., 1992a), aerobic exercise showed a significantly large antidepressant effect compared to routine practice treatment conditions (ES -0.82, CI95% -1.02 to -0.62, p=0.000, Q= 16.435, p=0.226, Begg tau -0.087, p=0.661, Egger intercept -0.754, p=0.567, I^2=20.88%).

Comparison to most common routine practice treatment forms: In the seven RCTs with control groups assigned to antidepressant or TAU (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015; Veale, Le Fevre, Pantelis et al., 1992a), aerobic exercise reduced depression by a significant, large effect-size (ES= -0.83, CI95% -1.05 to -0.61, p=0.000, Q= 3.180, p=0.786, Begg tau -0.000, p=1.000, Egger intercept -0.506, p=0.695, I^2=0%).

Comparison to antidepressant medication: In the four RCTs with antidepressant medication as control condition (George, Chandran. VV.Mohan and Sandesh, 2012; Legrand

and Neff, 2016; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007), aerobic exercise revealed a significantly large antidepressant impact (ES= -0.99, CI95% -1.30 to -0.68, p=0.000, Q= 0.654, p=0.884, Begg tau 0.166, p=0.734, Egger intercept 0.469, p=0.624, I^2=0%).

Comparison to singular control condition without concurrent treatments: Among the six RCTs with control groups assigned to singular condition without receiving concurrent treatment, aerobic exercise brought about a significant large antidepressant impact (George, Chandran. VV.Mohan and Sandesh, 2012; Legrand and Neff, 2016; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016) (ES= -0.94, CI95% -1.21 to -0.67, p=0.000, Q= 6.373, p=0.383, Begg tau -0.285, p=0.367, Egger intercept -0.654, p=0.662, I^2=5.85%).

Comparison to control groups on psychological conditions: In the five RCTs with control groups receiving psychological conditions either as the main assignment or as a concurrent treatment (Kerling, Tegtbur, Gützlaff et al., 2015; Martinsen, Medhus and Sandvik, 1985; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016; Veale, Le Fevre, Pantelis et al., 1992a), aerobic exercise displayed a significant, large reductive effect on depression(ES= -0.85, CI95% -1.21 to -0.48, p=0.000, Q= 8.641, p=0.124, Begg tau -0.400, p=0.259, Egger intercept -3.686, p=0.161, I^2=42.13%).

Comparison to all control groups excluding those on non-active conditions: In a total of ten RCTs with various control conditions (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015; Veale, Le Fevre, Pantelis et al., 1992a) excluding waiting list or self-managed psychological condition (Oertel-Knöchel, Mehler, Thiel et al., 2014; Sadeghi, Ahmadi, Ahmadi et al., 2016) aerobic exercise demonstrated a significantly large effect on depression (ES= -0.83, CI95% -1.05 to -0.60, p=0.000, Q= 12.265, p=0.132, Begg tau -0.136, p=0.537, Egger intercept -1.122, p=0.479, I^2=32.37%).

Outcomes

Self-rated or clinician-rated: Across the five RCTs with self-rated (Legrand and Neff, 2016; Martinsen, Medhus and Sandvik, 1985; Oertel-Knöchel, Mehler, Thiel et al., 2014; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016) and the seven RCTs with clinician-rated (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015;

Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015; Veale, Le Fevre, Pantelis et al., 1992a) outcome measures, aerobic exercise provided significant large antidepressant effect-sizes (self-rated: ES= -0.96, CI95% -1.34 to -0.58, p=0.000, Q= 6.810, p=0.235, Begg tau -0.133, p=0.707, Egger intercept -2.502, p=0.407, I^2=26.57%; clinician-rated: ES= -0.76, CI95% -0.99 to -0.53, p=0.000, Q= 8.746, p=0.271, Begg tau -0.107, p=0.710, Egger intercept 1.191, p=0.587, I^2=19.96%).

Study Design

Risk of Bias: Sensitivity evidence from four RCTs with top methodological scoring (PEDro scoring ≥7) (Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015) revealed a significantly moderate to large antidepressant effect for aerobic exercise (ES= -0.67, CI95% -1.03 to -0.30, p=0.000, Q= 6.338, p=0.175, Begg tau -0.100, p=0.806, Egger intercept -3.540, p=0.486, I^2=36.89%). Although no publication bias was revealed we computed trim and fill analysis (on both sides of the plot), which did not adjust the effect size. In the remaining RCTs with lower methodological quality scoring (PEDro scoring≤6)(George, Chandran. VV.Mohan and Sandesh, 2012; Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Oertel-Knöchel, Mehler, Thiel et al., 2014; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Sadeghi, Ahmadi, Ahmadi et al., 2016; Veale, Le Fevre, Pantelis et al., 1992a) aerobic exercise showed a significant, large antidepressant effect (ES= -0.91, CI95% -1.13 to -0.70, p=0.000, Q= 8.066, p=0.427, Begg tau -0.138, p=0.602, Egger intercept -0.481, p=0.711, I^2=0.81%).

Studies before or after 2012: Data polled from seven RCTs conducted over the last five years (George, Chandran. VV.Mohan and Sandesh, 2012; Kerling, Tegtbur, Gützlaff et al., 2015; Legrand and Neff, 2016; Oertel-Knöchel, Mehler, Thiel et al., 2014; Sadeghi, Ahmadi, Ahmadi et al., 2016; Salehi, Hosseini, Haghighi et al., 2016; Schuch, Vasconcelos-Moreno, Borowsky et al., 2015)documented significantly moderate to large antidepressant effects for aerobic exercise (ES= -0.73, CI95% -0.96 to -0.50, p=0.000, Q= 9.428, p=0.307, Begg tau 0.027, p=0.916, Egger intercept 1.072, p=0.528, I^2=15.15%). Similarly, significant large effects for aerobic exercise were recorded in the five RCTs conducted before 2012 (Martinsen, Medhus and Sandvik, 1985; Mota-Pereira, Silverio, Carvalho et al., 2011; Pilu, Sorba, Hardoy et al., 2007; Rueter, 1980; Veale, Le Fevre, Pantelis et al., 1992a) (ES= -1.02,

CI95% -1.39 to -0.65, p=0.000, Q= 5.408, p=0.248, Begg tau -0.500, p=0.220, Egger intercept -3.076, p=0.169, I^2=26.03%).

All sensitivity analyses are depicted in Supplementary Material-3.

Discussion

This meta-analysis has found that aerobic exercise compared to routine treatment conditions is related with a statistically significant large overall antidepressant effect with low and non-statistically significant heterogeneity (ES= -0.82, CI 95% -1.02 to -0.62 p=0.000, Q=16.435 p=0.226, Begg tau -0.087, p=0.661, Egger intercept -0.754, p=0.567, I^2=20.89%). Similarly, a significantly moderate to large effect was found in only trials with higher design scoring (≥7 on the PEDro scale) (ES= -0.67, CI95% -1.03 to -0.30, p=0.000, Q= 6.338, p=0.175, Begg tau -0.100, p=0.806, Egger intercept -3.540, p=0.486, I^2=36.89%). Also, aerobic exercise revealed a large or moderate to large effect when performed on short- or longer-term, under various settings or dropout rates, and across inpatients or outpatients with diverse symptom severity and age range. Therefore, aerobic exercise is considered an effective antidepressant intervention.

This study has various strengths. First, the large overall effect of aerobic exercise is congruent with other reviews with separate evaluations on clinical samples (Cooney, Dwan, Greig et al., 2013; Craft and Landers, 1998; Rethorst, Wipfli and Landers, 2009). Second, a comparable moderate to large effect was found in only trials with higher design quality scoring (≥7 on the PEDro scale). A similar findings was recorded by Rethorst, Wipfli and Landers (2009). To this extent, the anti-depressivenes of aerobic exercise is linked with lower rather than higher risk of bias. This is a major finding since risk of bias is inversely related with effectiveness (Moher, Pham, Jones et al., 1998; Schulz, 2001; Schulz, Chalmers, Hayes et al., 1995). Third, short-term aerobic exercise (up to 4 weeks) showed a large effect, highlighting its important role at the early stage of care as the most frequently prescribed treatment of pharmacotherapy is typically requiring at comparable period of time before providing any benefit (Eisenberg, Center for Clinical Decisions and Communications Science, 2011; Gartlehner, Hansen, Morgan et al., 2011; Seehusen and Sheridan, 2013). Fourth, the large effect of aerobic exercise performed on longer-term (9-12 weeks) ~~or~~ for 3 times/week is in line with treatment guidelines for depression recommending physical activity of 3 times/week for a period of 12 weeks-(on average) (National Institute for Clinical Excellence [NICE], 2009). Fifth, aerobic exercise revealed a pluralistic adaptability. It provided a relief in

depression in outdoor and indoor settings, under group or individualised settings, and across groups with higher or lowerdropout rates from exercise. Sixth, the effect of aerobic exercise was associated with increased generalizability; depression was improved in outpatients or inpatients, and in groups with more women or men, with younger or mature adults, or with different depression symptom severity. Noteworthy, 33% of reviewed trials with severely depressed patients consisted of treatment-resistant depressed patients. Seventh, when trialists involved aspects of preference-based exercising, aerobic exercise manifested antidepressant effects. Exercising through or based on individual preferences seems to be a promising strategy(Callaghan, Khalil, Morres et al., 2011; Morres, Stathi, Martinsen et al., 2014; Morton, Biddle and Beauchamp, 2008).

The eight strength of this study is the inclusion of only trials with patients from mental health services. Previous reviews have included a number of trials with psychometrically defined depressed persons recruited via media advertising. Media respondents, however, may have strong outcome expectations, and a non-clinical depression despite high psychometric scores in checklists of depression or a possible diagnosis at study entry. Depressed patients instead, have suffered tenacious symptoms including psychosocial impairment that led to a health service. Also, they may often cope with disappointment or frustration as the mental health services use uncovers not only the disease severity, but also the need for systematic care (Bursztajn and Barsky, 1985; Maguire, Cullen, O'Sullivan et al., 1995; Morgan, 1989). Thus, depressed patients recruited via health services have a more challenging profile compared to media respondents. Meta-analyses with subgroup analyses on clinical samples have reported similar findings to our study including significantly moderate effects for exercise (Cooney, Dwan, Greig et al., 2013) or large (Craft and Landers, 1998; Rethorst, Wipfli and Landers, 2009), in the latter study (Rethorst, Wipfli and Landers, 2009) the large effect-size became even larger and remained significant after coding for risk of bias. The ninth strength of this study refers to the inclusion of only adult depressed patients aged 18-65 years old. This separation appeared to be essential given that elderly depressed patients in comparison to adult depressed patients show distinct clinical differences in depression (Fiske, Wetherell and Gatz, 2009) and higher depression relief through exercise(Silveira, Moraes, Oliveira et al., 2013).

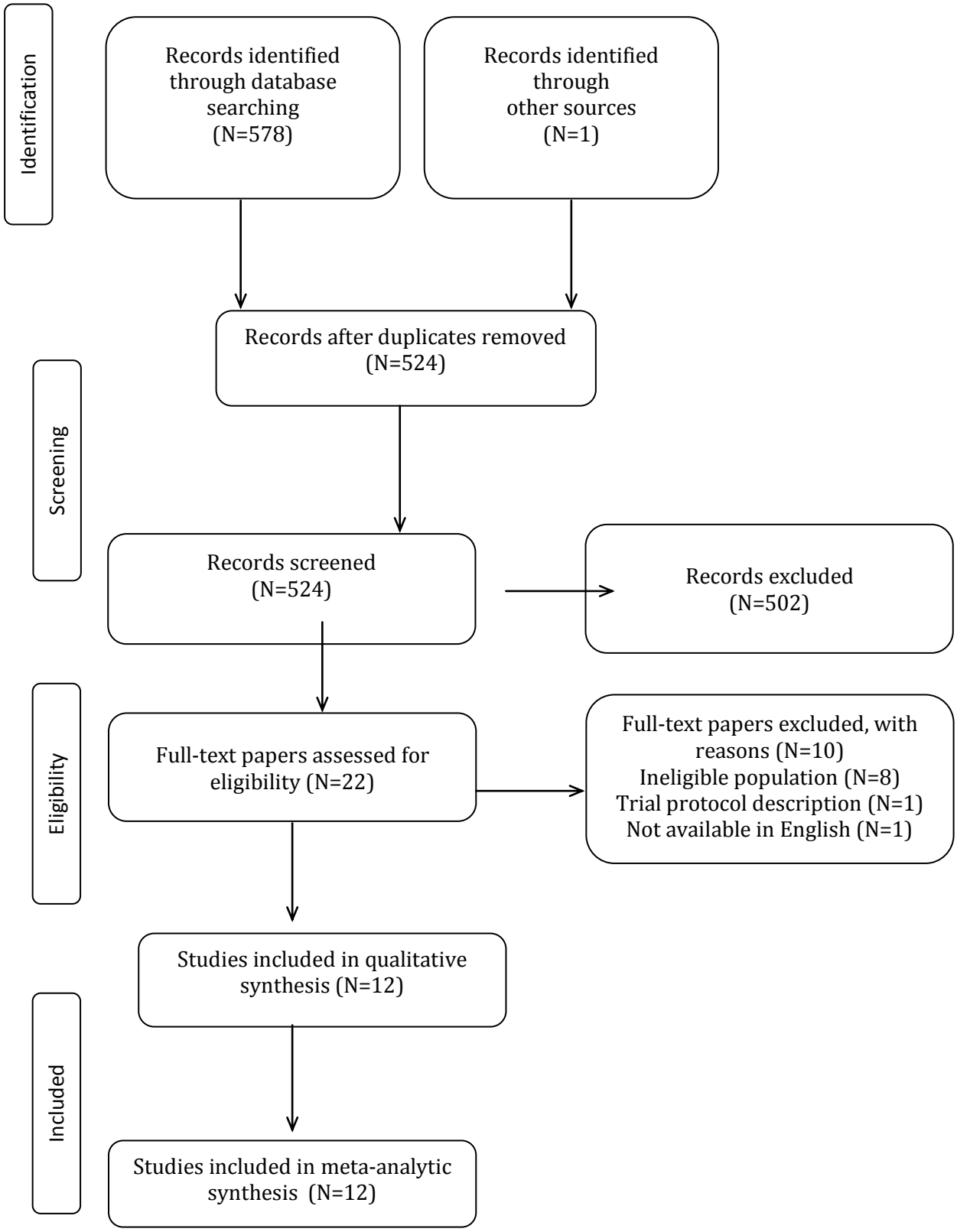
The final strength refers to the clinically meaningful antidepressant effect of aerobic exercise. Across the four fully supervised-based exercise trials that used the outcome measure of HAMD, we found a reduction in depression score by 3.7 points (-3.69, CI= -5.104, -2.289, standard error= 0.718, $p<0.001$). Also, depression scores was reduced by almost 11 points (-

10.82, CI=-14.06, -7.57, standard error=1.656, $p<0.001$) in the four supervised-based exercise trials that employed the BDI scale. These reductions are considered clinically meaningful by the National Institute for Health and Care Excellence (NICE) (National Institute for Clinical Excellence [NICE], 2009), as the relevant cutoff score is 3 points.

The major limitation of this study is the inclusion of a small number of trials, a widely seen limitation in exercise reviews on depression. However, we run a robust analysis to offset threats caused by publication bias. Also, most of the sensitivity analyses involved consideration that at least five trials are essential to avoid imprecise results.

This is the first study to examine the antidepressant impact of aerobic exercise in exclusively adult depressed patients (18-65) recruited through health services and not through media advertisements. Notwithstanding the small number of trials reviewed, it is concluded that moderate intensity of supervised-based aerobic exercise delivered three 3 times/week for both short- (up to 4 weeks) and longer-term (8-12 weeks) compared favourably to routine practice treatment forms showing profound anti-depressiveness. Hence, guidelines for the treatment of depression recommending moderate intensity structured exercise programmes 3 times/week for a period of 10-14 weeks continue to represent the cornerstone of exercise on prescription schemes (National Institute for Clinical Excellence [NICE], 2009). Our study is, therefore, reporting that aerobic exercise is considered a valuable antidepressant intervention in routine practice treatment forms.

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.



Supplementary Material-1. PEDro Consensus Scores of randomized controlled trials

PEDro Criteria	Random Allocation	Allocation Concealment	Balance Baseline	Blinding patient/therapist/assessor	Drop-outs (<15%)	Intention to treat	Statistical comparison between groups	Point/variability measures	PEDro Total
RCTs									
Schuch et al., 2015	1	1	1	0/0/1	1	1	1	1	8
Kerling et al., 2015	1	1	1	0/0/1	1	1	1	1	8
Legrand and Neff 2016	1	1	1	0/0/0	1	1	1	1	7
Salehi et al., 2016	1	1	0	0/0/1	1	1	1	1	7
Pilu et al., 2007	1	0	1	0/0/0	1	1	1	1	6
Mota-Pereira et al., 2011	1	1	0	0/0/1	1	0	1	1	6
George et al., 2012	1	0	1	0/0/1	0	0	1	1	5
Oertel-Knöchel et al., 2014	1	0	0	0/0/1	0	1	1	1	5
Martinsen et al., 1985	1	0	1	0/0/0	1	1	1	0	5
Sadeghi et al., 2016	1	0	1	0/0/1	0	0	1	1	5
Veale et al., 1992a	1	0	1	0/0/0	0	0	1	1	4
Rueter, 1980	1	0	1	0/0/0	0	0	1	1	4

PEDro: Physiotherapy Evidence-based Database scale RCTs: randomized controlled trials

Supplementary Material-2. Description of randomized controlled trials

Trials	Interventions	N/ ♀ %	age m/sd (yrs)	attendance drop-outs %	strength vo_2max	concurrent psychiatric therapies %	depression primary outcome pre/post	PEDro consensus score
Mota-Pereira et al., 2011	Outpatients, 10males, 19 females							
	A. Aerobic Exercise (more depressed on the HAMD-17)	22/	48.6/	91%	---	100[A]	HAMD-17	
	Walking 30-45min/5times/week/12weeks; individual/supervised weekly session by a sport scientist at hospital gymnasium on a treadmill, 5.0km/h/0° grade equal to 3.7-4 metabolic equivalents (moderate intensity). Home-based walking 4times/week, intensity prescription via accelerometers (>1952 counts) or perceived exertion (e.g., no shortness of breath). Compliance support: reminders, staff emphasized the exercise benefits, consulted family members on social support for exercise.	57.9	2.3	14	---		severe/ improved to mild[§,†]	6
	B. Usual pharmacotherapy (control group) (more depressed)	11/	45.3/	---	---	---	mild/unimproved	
	Non-sedating antidepressants	80	3.1	9	---			
	MIC: treatment resistance after 9-15 months of combined pharmacotherapy, no regular exercising, no psychotherapeutic treatment, no change in medication in the last 6weeks, age range 18-60 years							
Veale et al., 1992a	outpatients, mean age 35.5, 3times/week/12weeks							
	A. Aerobic Exercise	48/	---	---	---	45[A]	CIS	
	Group/supervised running in a public park just outside hospital. Warm-up and stretching before running.	---	---	25	A[§]	100[P]	moderate-severe/ improved [§,†]	4
	B. Treatment as usual (control group)	35/	---	---	---	34[A]	moderate-severe/	
	Supportive psychotherapy.	---	---	17.2	B		improved[§]	
	MIC: >17 total weighted score&>2 depression severity score on the CIS							
Schuchet al., 2015	inpatients, mean age 40.30 years, early phase (24hours) of hospitalisation							
	A. Aerobic Exercise	25/	38.8/	---	---	80[A]	HAMD-17	
	Self-selected type of exercise (stationary bicycle, treadmill, or stepper) and intensity 3times/week for 3weeks provided that 16kcal/kg/week are completed. Individual/supervised at hospital.	72	11.5	8	---	8[ECT]	severe/ improved to normal[§,†]	8
	B. Treatment as usual (control group)	25/	41.7/	---	---	---	severe/	
	All patients were prescribed antidepressants. ECT was prescribed to 8% of the patients.	76	10.4	4	---	---	improved to mild[§]	
	MIC: a score of ≥25 on HAMD-17							

Trials	Interventions	N/ ♀ %	age m/sd (yrs)	attendance drop-outs %	strength vo_2max	concurrent psychiatric therapies %	depression primary outcome pre/post	PEDro consensus Score
Martinsen et al., 1985	inpatients, mean age 40, age range 17-60 years, 60min/3times/week/9weeks							
	A. Aerobic Exercise Group-based/supervised outdoor jogging & walking at 50-70% vo_2max supplemented by bicycling and/or swimming sessions at the patient's preference.	28/ ---	--- ---	--- 14.2	--- A[§ †]	32^{A} $100^{P,OT}$	BDI moderate/improved to mild[§†]	5
	2.Occupational Therapy (control group) All patients on group-based occupation therapy.	21/ ---	--- ---	--- 10.5	--- B	66^{A} 100^{P}	moderate/ improved[§]	
						MIC: both males and females		
Reuter, 1980	outpatients, undergraduate students, age range 18-30 years, 82% females							
	A. Aerobic Exercise Individual/supervised (co-running) running for at least 20min 3times/week/10 weeks (public indoors sport track). Pace allowed talking, non-competitive, no distance/speed criteria.	11/ ---	--- ---	--- 18	--- ---	$100^{C,†}$	BDI moderate/ improved tominimal[§,†]	4
	B. Counselling Therapy (control group) Group & individual counselling for 10weeks, at least 30min/week. Also, on waiting list for joining in the aerobic exercise program.	11/ ---	--- ---	--- 18	--- ---	---	moderate/unimproved[§]	
						MIC: a score of >15 on BDI		

Trials	Interventions	N/ ♀ %	age m/sd (yrs)	attendance drop-outs %	strength vo_2max	concurrent psychiatric therapies %	depression primary outcome pre/post	PEDro consensus Score
Oertel-Knöchel et al., 2014	intpatients, mean age 40.00 (SD=14.10), in hospital							
	A. Aerobic exercise Group-based, supervised, 3 times/week/4weeks for 45min at 60-70%MHR. Warm-up for 10min, 25min cardio training (aerobic exercise, aerobic with boxing exercises and circuit training) and 10min cool-down.	8/ 50	36.63/ 12.91		--- ---	100[CT]	BDI moderate/improved to mild-moderate[§]	
	B. Relaxation Group-based, supervised, breathing exercises, "enjoy exercises", "imaginary journey", relaxation or acceptance and awareness training 3times/week/4weeks for 45min. No yoga, no muscle progressive relaxation was applied.	6/ 66	41.37/ 15.69	drop outs: 32% across all groups	--- ---	100[CT]	moderate/improved[§]	5
	C. Waiting (control) No intervention	8/ 38	42.21/ 8.31		--- ---	---	moderate/not improved	
				MIC: stable medication 1 month before and during the trial, disease duration at least 5years				
Kerling et al., 2015	inpatients							
	A. Aerobic exercise Group-based, supervised by study nurses, 3times/week/6weeks for 51min at moderate intensity and at 13max at the Borg scale. Warm up for 6min, 25min on a bicycle ergometer, and 20min at personal preference on arm ergometer, cross trainer, stepper, treadmill, recumbent, or rowing ergometer.	22/ 45	44.20/ 8.50	>90 0	--- ---	77[A] 100[CBT]	MADRS moderate-severe/ improved to mild-moderate[§]	
	B. Treatment as usual Antidepressant drugs and cognitive behavioural therapy were prescribed to 75% and 100% of the patients, respectively. All patients attended a supervised daily moderate physical activity programme of ball games, walking, and stretching for 20min.	20/ 30	40.90/ 11.90	--- 0	--- ---	75 [A] 100[CBT]	moderate-severe/ improved to mild-moderate[§]	8
				MIC: no acute/chronic infectious disease, no acute/lifetime immunological disease				

Trials	Interventions	N/ ♀ %	age m/sd (yrs)	attendance drop-outs %	strength vo_2max	concurrent psychiatric therapies %	depression primary outcome pre/post	PEDro consensus Score
Sadeghi et al., 2016	outpatients, undergraduate students, 36males, 10 females							
	A. Aerobic exercise Supervised 50-60min/8 weeks. Warm up 10min with stretching, breathing, various exercises of upper/lower limbs, and running in place at low intensity. The same exercises with greater intensity at 60-80%MHR for 30-35min. The same exercisers with lower intensity for 10-15min as a cooling down phase.	16/ 81	20.93/ 1.06	--- ---	--- ---	No	BDI moderate/improved to mild[§, †] (A>C)	
	B. Cognitive Therapy Cognitive therapy for 8 weeks, 2 times/week in the first 4 weeks, and 1 time/week in the remaining 4 weeks.	16/ 75	21.12/ 1.25	--- ---	--- ---	No	moderate/improved to mild[§, †] (B>C)	5
	C. Group meetings (control group) Group meetings of 45-60min for 8 weeks to discuss issues raised by the group members themselves.	14/ 79	20.92/ 1.20	--- ---	--- ---	No	moderate/not improved	
							MIC: BDI score 13-28, no medication	
Salehi et al., 2016	inpatients, mean age 29.67 (SD=5.81), 30% females							
	A. Aerobic exercise Individual/supervised (by nurses) cycling/treadmill 3times/week/ 4weeks for 40-45min/session at 60-75% VO2max, in the clinic.	20/ 25	29.05/ 5.11	100 0	--- ---	100[A]	HAMD-17 severe/improved to mild[§]	
	B. Electroconvulsive Therapy ECT 3times/week/4weeks.	20/ 35	29.7/ 6.28	100 0	--- ---	100[A]	severe/improved to mild[§]	7
	C. Aerobic Exercise and Electroconvulsive Therapy Both aerobic exercise and ECT as described above.	20/ 35	30.25/ 6.21	100 0	--- ---	100[A]	severe/improved to normal-mild[§]	
							MIC: age 25 to 40, HAMD score of >2	
Pilu et al., 2007	outpatients, age range 40-60 years, 100% females							
	A. Aerobic Exercise Group/supervised training for 60min/2times/week/32weeks. 5min warm up, 50min on a self-selected cardio-fitness machine change every 4min (20 options), 5min cooling down/stretching. Location: Community-based gym. Supervisor was qualified in sport, psychology and sport psychopathology.	10/ 100	--- ---	--- 0	--- ---	100[A]	HAMD-17 severe/ improved to normal-mild[§, †]	6
	B. Pharmacotherapy (control group) 70% & 10% of the patients on SSRIs and SNRIs, respectively, 5% of the patients on SSRI + SNRI + Tricyclic antidepressants.	20/ 100	--- ---	--- 0	--- ---	---	severe/ unimproved	
							MIC: female, 2month persistence of score of >13 on HAMD-17 despite medication, 40-60 years	

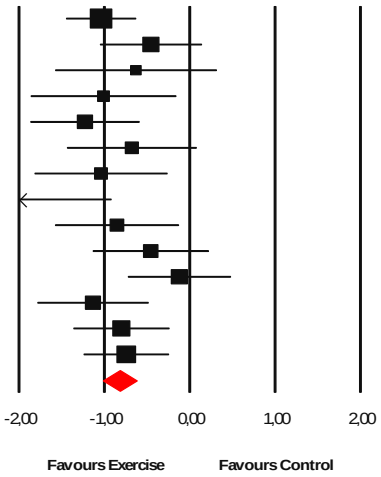
Trials	Interventions	N/ ♀ %	age m/sd (yrs)	attendance drop-outs %	strength vo_2max	concurrent psychiatric therapies %	depression primary outcome pre/post	PEDro consensus Score
Legrand and Neff, 2016	intpatients, mean age 45.30 (SD=13.20), 71% females							
	A. Aerobic exercise Supervised/individual daily brisk walking or jogging of 30min/10days in a park outside the hospital. Most sessions (92%) were individual.	14/ 64.3	45.30/ 10.06	--- 7.1	--- ---	100[A]	BDI severe/improved to mild-moderate [§, †] (A>C)	
	B. Stretching exercise Supervised daily stretching for 30min/10days on muscle groups (thighs, calves, gluteal, shoulders, and back) in a hospital room. Muscles groups were stretched for 60secs with equivalent break.	11/ 72.7	41.08/ 13.2	--- 18	--- ---	100[A]	severe/improved[§]	7
	C. Control group All patients were treated with antidepressant medication; 70% on SSRI's, 20% on SSNRI's, and 10% on dopamine agonist.	10/ 70	49.10/ 16.50	--- 10	--- ---	---	severe/not improved	
		MIC: BDI score of >28, patients treated with antidepressants, antidepressant drug therapy initiated <2 weeks before participation in the trial						
George et al., 2012	outpatients, age range 18-39 years, 100% males							
	A. Aerobic exercise Group-based supervised 45min/3times/week/12weeks. Warm up of 5min walk and 5min stretch in major muscles, followed by 10min brisk walking at 60%MHR, 10min jogging at 70%MHR and by 10min running at 80%MHR. Cool-down of progressive speed reduction for 5min.	50/ 0	--- ---	--- 0	--- ---	100[A] ---	HAMD-17 mild-moderate / improved to mild[§, †]	5
	B. Antidepressant medication (control) All patients were prescribed antidepressant medication.	50/ 0	--- ---	--- 0	--- ---	--- ---	mild-moderate / improved to mild[§]	
		MIC: 18-39 years old, HAMD score of >13, no participation in exercise over the last 12 months						

A: antidepressants, AME: abdominal muscle endurance, BDI: Beck Depression Inventory, BRMS: Bech-Rafaelsen Melancholy Scale, CBT: Cognitive Behavioral Therapy, CIS: Clinical Interview Schedule, C: counselling, CT: Cognitive training, ECT: electroconvulsive therapy, HAMD-17: Hamilton Rating Scale Depression, Max: maximum, MIC: Major Inclusion Criteria, MHR: maximum heart rate, MHRR: maximum heart rate reserve, MADRS: Montgomery-Åsberg Depression Rating Scale, OT: occupational therapy, P: psychotherapy, PS: Psychological therapies, Rep: repetition, SCL-90: Symptom Checklist-90, SD: standard deviation, SDS: Self-rating Depression Scale, SNRI: serotonin-norepinephrine reuptake inhibitor, SSRI: selective serotonin reuptake inhibitor, Vo_2max: maximum aerobic capacity, §: Statistically significant difference within group, †: Statistically significant difference between groups

Supplementary Material-3. Meta-analytic results

Aerobic Exercise vs. controls on routine practice treatment conditions (overall effect)

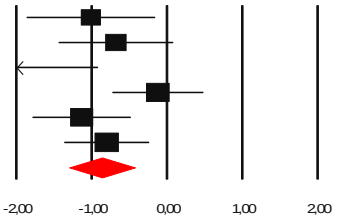
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
George 2012	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Pilu 2007	-1,04	0,40	0,16	-1,82	-0,25	-2,60	0,01
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Sadeghi 2016a	-0,85	0,37	0,14	-1,58	-0,12	-2,29	0,02
Sadeghi 2016b	-0,46	0,35	0,12	-1,14	0,23	-1,31	0,19
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
Veale 1992	-0,74	0,26	0,07	-1,25	-0,24	-2,89	0,00
	-0,82	0,10	0,01	-1,02	-0,63	-8,15	0,00



Meta Analysis

Individual-Based Aerobic Exercise

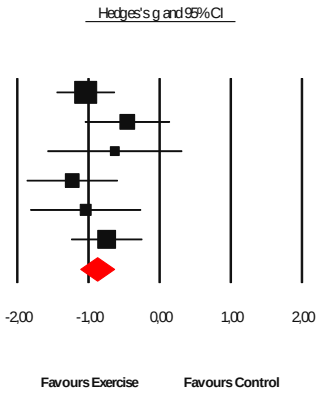
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
	-0,87	0,22	0,05	-1,30	-0,43	-3,89	0,00



Meta Analysis

Group Based Aerobic Exercise

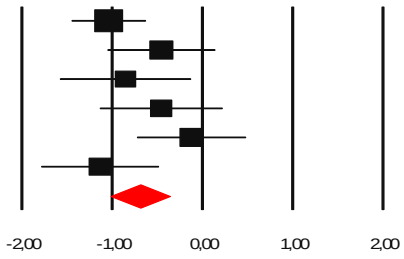
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
George 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Pilu 2007	-1,04	0,40	0,16	-1,82	-0,25	-2,60	0,01
Veale 1992	-0,74	0,26	0,07	-1,25	-0,24	-2,89	0,00
	-0,88	0,12	0,01	-1,12	-0,64	-7,25	0,00



Meta Analysis

Males

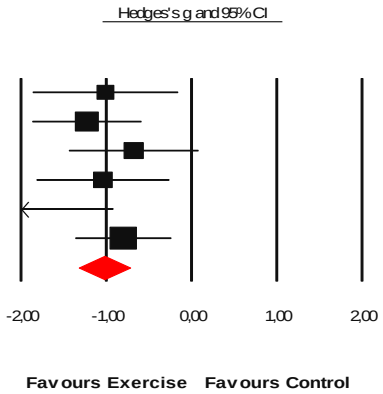
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Gerorge 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Sadeghi 2016a	-0,85	0,37	0,14	-1,58	-0,12	-2,29	0,02
Sadeghi 2016b	-0,46	0,35	0,12	-1,14	0,23	-1,31	0,19
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
	-0,69	0,17	0,03	-1,02	-0,37	-4,14	0,00



Meta Analysis

Females

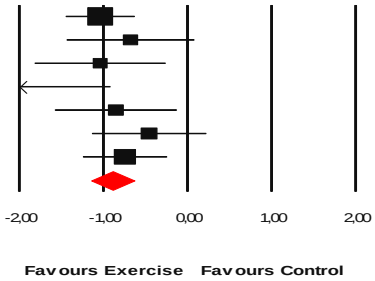
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Pilu 2007	-1,04	0,40	0,16	-1,82	-0,25	-2,60	0,01
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
	-1,03	0,15	0,02	-1,33	-0,73	-6,68	0,00



Meta Analysis

Outpatients

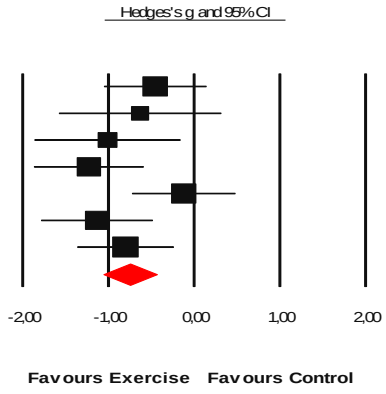
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Gerorge 2011	-1,038	0,212	0,045	-1,453	-0,623	-4,906	0,000
Mota-Perreira 2011	-0,678	0,390	0,152	-1,442	0,087	-1,737	0,082
Pilu 2007	-1,039	0,400	0,160	-1,823	-0,255	-2,597	0,009
Reuter 1980	-2,010	0,560	0,314	-3,108	-0,912	-3,588	0,000
Sadeghi 2016a	-0,852	0,373	0,139	-1,582	-0,122	-2,286	0,022
Sadeghi 2016b	-0,456	0,349	0,122	-1,141	0,228	-1,306	0,192
Veale 1992	-0,744	0,257	0,066	-1,248	-0,239	-2,888	0,004
	-0,894	0,131	0,017	-1,152	-0,637	-6,807	0,000



Meta Analysis

Inpatients

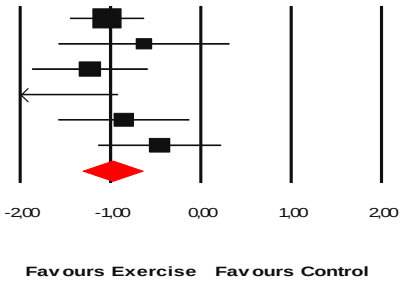
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
	-0,75	0,16	0,03	-1,06	-0,44	-4,74	0,00



Meta Analysis

Mild-Moderate to Moderate Deperssion Severity

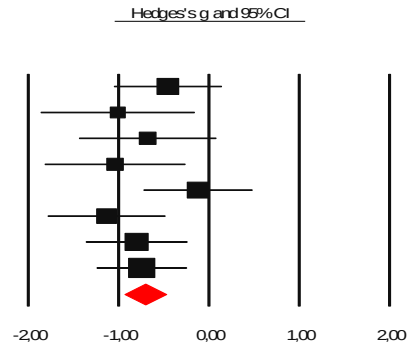
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Gerorge 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Sadeghi 2016a	-0,85	0,37	0,14	-1,58	-0,12	-2,29	0,02
Sadeghi 2016b	-0,46	0,35	0,12	-1,14	0,23	-1,31	0,19
	-0,98	0,17	0,03	-1,31	-0,65	-5,81	0,00



Meta Analysis

Moderate-Severe to Severe Deperssion Severity

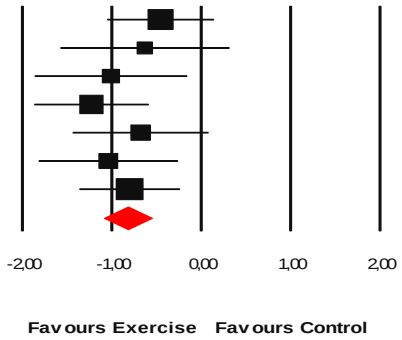
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Pilu 2007	-1,04	0,40	0,16	-1,82	-0,25	-2,60	0,01
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
Veale 1992	-0,74	0,26	0,07	-1,25	-0,24	-2,89	0,00
	-0,71	0,12	0,01	-0,94	-0,48	-6,07	0,00



Meta Analysis

Age Range 40-65 years

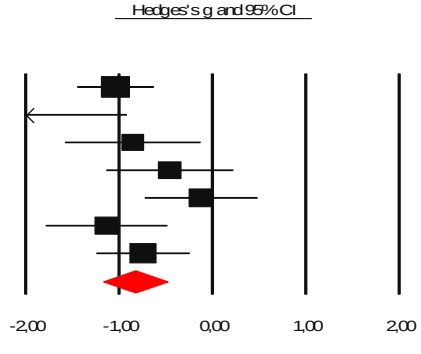
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Pilu 2007	-1,04	0,40	0,16	-1,82	-0,25	-2,60	0,01
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
	-0,82	0,14	0,02	-1,09	-0,56	-6,06	0,00



Meta Analysis

Age Range 18-39 years

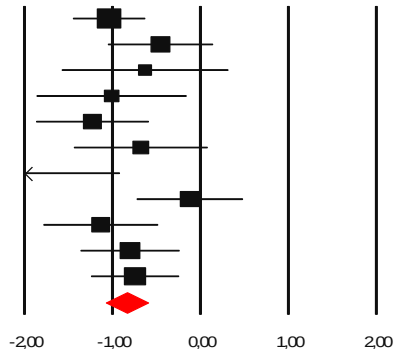
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Gerorge 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Sadeghi 2016a	-0,85	0,37	0,14	-1,58	-0,12	-2,29	0,02
Sadeghi 2016b	-0,46	0,35	0,12	-1,14	0,23	-1,31	0,19
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Veale 1992	-0,74	0,26	0,07	-1,25	-0,24	-2,89	0,00
	-0,83	0,18	0,03	-1,18	-0,49	-4,72	0,00



Meta Analysis

Aerobic Exercise three times per week

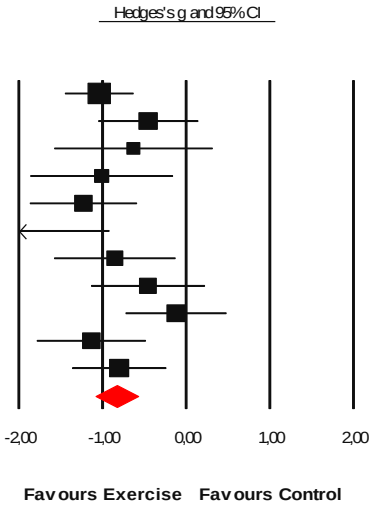
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
George 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
Veale 1992	-0,74	0,26	0,07	-1,25	-0,24	-2,89	0,00
	-0,84	0,12	0,01	-1,08	-0,60	-6,88	0,00



Meta Analysis

Aerobic Exercise of 45 minutes on average

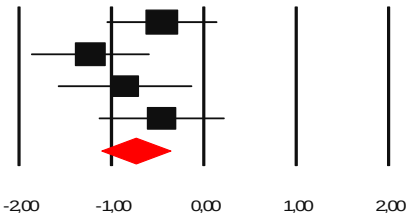
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
George 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Sadeghi 2016a	-0,85	0,37	0,14	-1,58	-0,12	-2,29	0,02
Sadeghi 2016b	-0,46	0,35	0,12	-1,14	0,23	-1,31	0,19
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
	-0,83	0,13	0,02	-1,09	-0,58	-6,43	0,00



Meta Analysis

Aerobic Exercise of 45 to 60 minutes

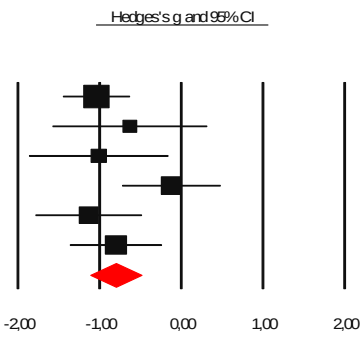
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Sadeghi 2016a	-0,85	0,37	0,14	-1,58	-0,12	-2,29	0,02
Sadeghi 2016b	-0,46	0,35	0,12	-1,14	0,23	-1,31	0,19
	-0,74	0,19	0,04	-1,11	-0,37	-3,89	0,00



Meta Analysis

Aerobic Exercise of 30 to 45 minutes

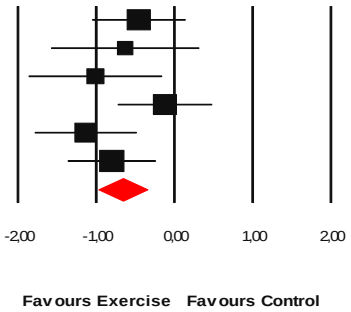
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
George 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
	-0,81	0,16	0,03	-1,12	-0,49	-5,04	0,00



Meta Analysis

Aerobic Exercise of up to six weeks

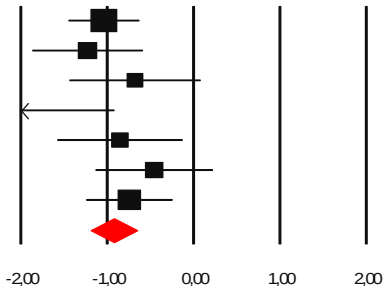
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
	-0,66	0,16	0,03	-0,97	-0,35	-4,16	0,00



Meta Analysis

Aerobic Exercise eight to twelve weeks

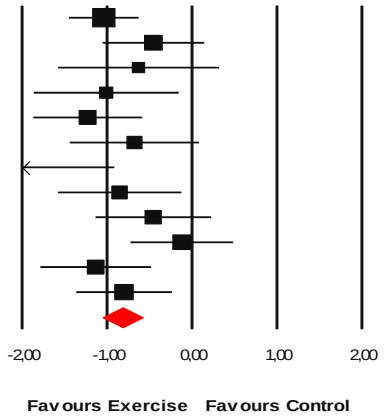
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
George 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Sadeghi 2016a	-0,85	0,37	0,14	-1,58	-0,12	-2,29	0,02
Sadeghi 2016b	-0,46	0,35	0,12	-1,14	0,23	-1,31	0,19
Veale 1992	-0,74	0,26	0,07	-1,25	-0,24	-2,89	0,00
	-0,93	0,14	0,02	-1,20	-0,66	-6,74	0,00



Meta Analysis

Aerobic Exercise of of moderate intensity

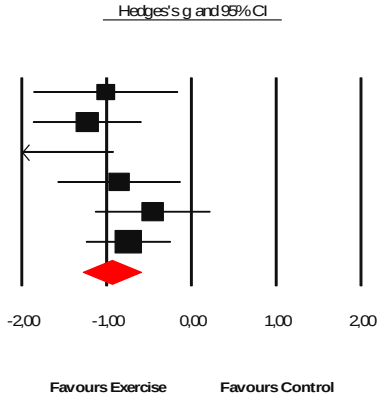
Studyname	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
George 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Sadeghi 2016a	-0,85	0,37	0,14	-1,58	-0,12	-2,29	0,02
Sadeghi 2016b	-0,46	0,35	0,12	-1,14	0,23	-1,31	0,19
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
	-0,82	0,12	0,01	-1,06	-0,59	-6,85	0,00



Meta Analysis

Equipment-free Aerobic Exercise

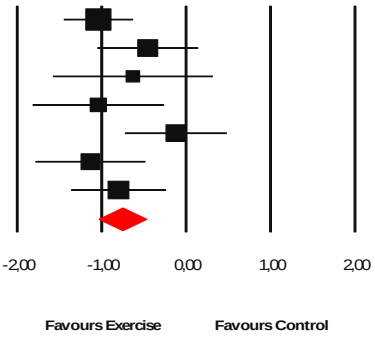
Studyname	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Sadeghi 2016a	-0,85	0,37	0,14	-1,58	-0,12	-2,29	0,02
Sadeghi 2016b	-0,46	0,35	0,12	-1,14	0,23	-1,31	0,19
Veale 1992	-0,74	0,26	0,07	-1,25	-0,24	-2,89	0,00
	-0,94	0,17	0,03	-1,29	-0,60	-5,39	0,00



Meta Analysis

Equipment-based Aerobic Exercise

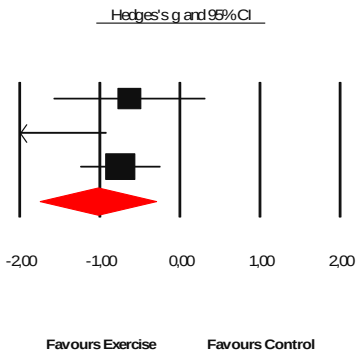
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
George 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Pilu 2007	-1,04	0,40	0,16	-1,82	-0,25	-2,60	0,01
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
	-0,76	0,14	0,02	-1,04	-0,48	-5,26	0,00



Meta Analysis

Aerobic Exercise - Dropouts rates equal or more than 15%

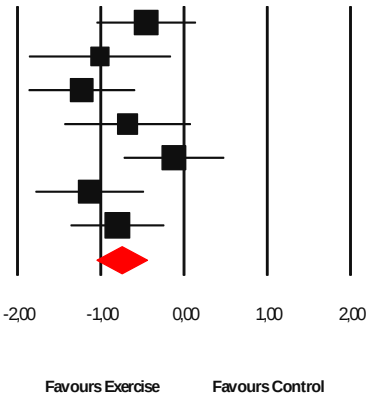
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Veale 1992	-0,74	0,26	0,07	-1,25	-0,24	-2,89	0,00
	-1,03	0,37	0,14	-1,75	-0,30	-2,77	0,01



Meta Analysis

Aerobic Exercise - Dropouts rates less than 15%

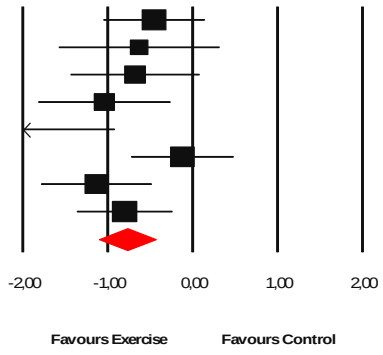
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
	-0,75	0,15	0,02	-1,06	-0,45	-4,87	0,00



Meta Analysis

Indoor-based Aerobic Exercise

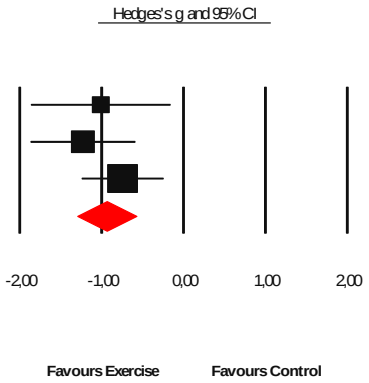
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Pilu 2007	-1,04	0,40	0,16	-1,82	-0,25	-2,60	0,01
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
	-0,77	0,17	0,03	-1,11	-0,44	-4,54	0,00



Meta Analysis

Outdoor-based Aerobic Exercise

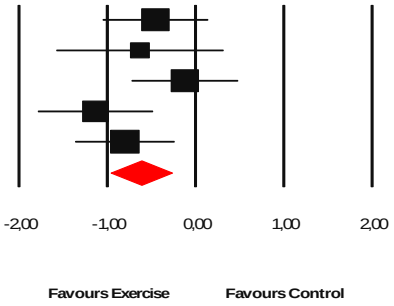
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Veale 1992	-0,74	0,26	0,07	-1,25	-0,24	-2,89	0,00
	-0,94	0,18	0,03	-1,30	-0,58	-5,12	0,00



Meta Analysis

Hospital-based Aerobic Exercise

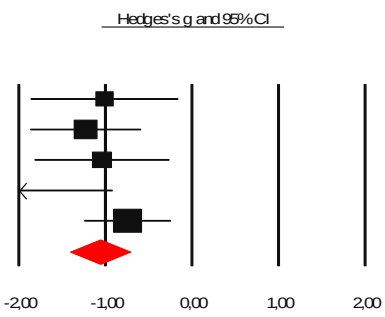
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
	-0,62	0,18	0,03	-0,97	-0,27	-3,50	0,00



Meta Analysis

Aerobic Exercise Outside Hospital

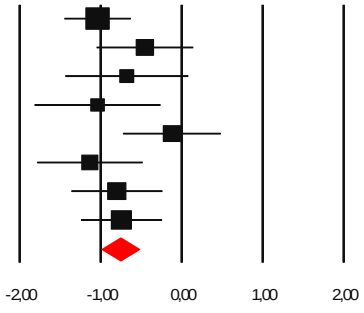
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Pilu 2007	-1,04	0,40	0,16	-1,82	-0,25	-2,60	0,01
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Veale 1992	-0,74	0,26	0,07	-1,25	-0,24	-2,89	0,00
	-1,07	0,18	0,03	-1,41	-0,72	-6,03	0,00



Meta Analysis

Clinician-rated Depression

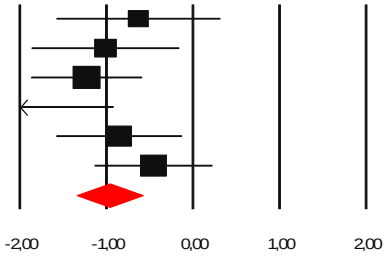
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
George 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Pilu 2007	-1,04	0,40	0,16	-1,82	-0,25	-2,60	0,01
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
Veale 1992	-0,74	0,26	0,07	-1,25	-0,24	-2,89	0,00
	-0,76	0,12	0,01	-0,99	-0,53	-6,44	0,00



Meta Analysis

Self-rated Depression

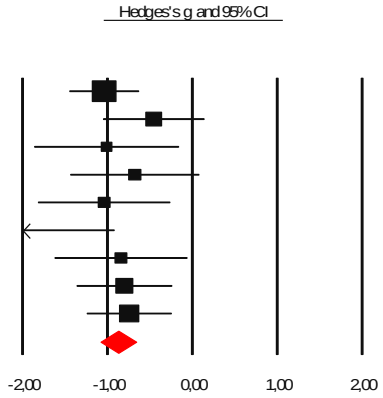
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Sadeghi 2016a	-0,85	0,37	0,14	-1,58	-0,12	-2,29	0,02
Sadeghi 2016b	-0,46	0,35	0,12	-1,14	0,23	-1,31	0,19
	-0,97	0,19	0,04	-1,35	-0,59	-4,98	0,00



Meta Analysis

Aerobic Exercise VS most common treatments (TAU or medication)

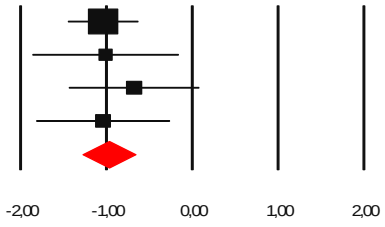
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
George 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Pilu 2007	-1,04	0,40	0,16	-1,82	-0,25	-2,60	0,01
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Schuch 2011	-0,84	0,40	0,16	-1,63	-0,05	-2,09	0,04
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
Veale 1992	-0,74	0,26	0,07	-1,25	-0,24	-2,89	0,00
	-0,88	0,11	0,01	-1,09	-0,67	-8,19	0,00



Meta Analysis

Aerobic Exercise vs. Antidepressant Medication

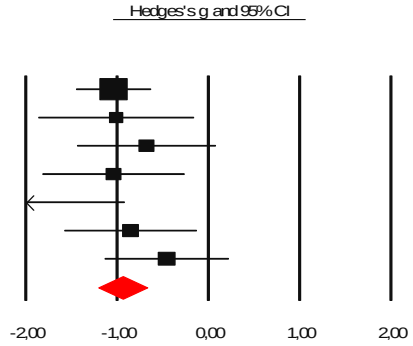
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
George 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Pilu 2007	-1,04	0,40	0,16	-1,82	-0,25	-2,60	0,01
	-0,98	0,16	0,02	-1,28	-0,67	-6,20	0,00



Meta Analysis

Aerobic Exercise vs. singular control condition wihtout concurrent treatments

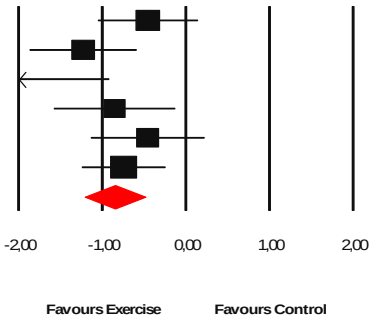
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
George 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Pilu 2007	-1,04	0,40	0,16	-1,82	-0,25	-2,60	0,01
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Sadeghi 2016a	-0,85	0,37	0,14	-1,58	-0,12	-2,29	0,02
Sadeghi 2016b	-0,46	0,35	0,12	-1,14	0,23	-1,31	0,19
	-0,94	0,14	0,02	-1,21	-0,68	-6,91	0,00



Meta Analysis

Aerobic Exercise vs. controls on psychol therapies

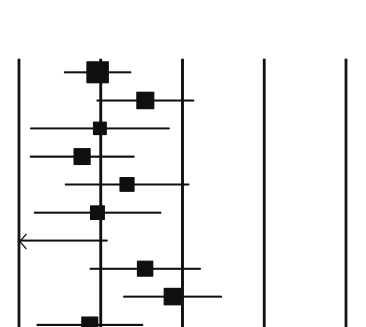
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Kerling 2015	-0,454	0,307	0,094	-1,056	0,148	-1,479	0,139
Martinsen 1985	-1,227	0,329	0,108	-1,873	-0,582	-3,729	0,000
Reuter 1980	-2,010	0,560	0,314	-3,108	-0,912	-3,588	0,000
Sadeghi 2016a	-0,852	0,373	0,139	-1,582	-0,122	-2,286	0,022
Sadeghi 2016b	-0,456	0,349	0,122	-1,141	0,228	-1,306	0,192
Veale 1992	-0,744	0,257	0,066	-1,248	-0,239	-2,888	0,004
	-0,852	0,185	0,034	-1,214	-0,489	-4,607	0,000



Meta Analysis

Aerobic Exercise vs. Controls on active treatment conditions

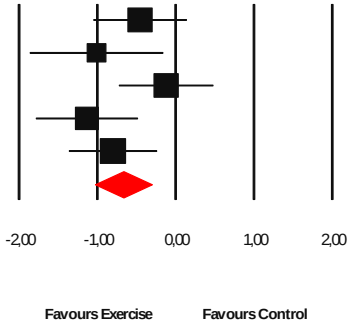
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
George 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Pilu 2007	-1,04	0,40	0,16	-1,82	-0,25	-2,60	0,01
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Sadeghi 2016b	-0,46	0,35	0,12	-1,14	0,23	-1,31	0,19
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
Veale 1992	-0,74	0,26	0,07	-1,25	-0,24	-2,89	0,00
	-0,83	0,12	0,01	-1,06	-0,61	-7,23	0,00



Meta Analysis

Aerobic Exercise in trials with top methodological quality (PEDro= 7 or 8)

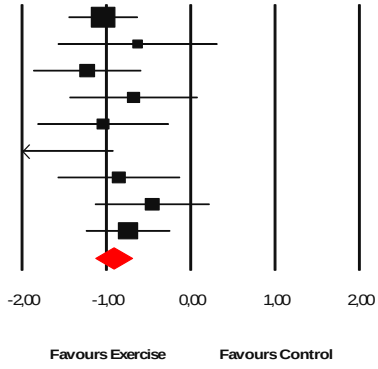
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
	-0,67	0,19	0,03	-1,03	-0,31	-3,62	0,00



Meta Analysis

Aerobic Exercise in trials with lower methodological quality (PEDro= 6 or less)

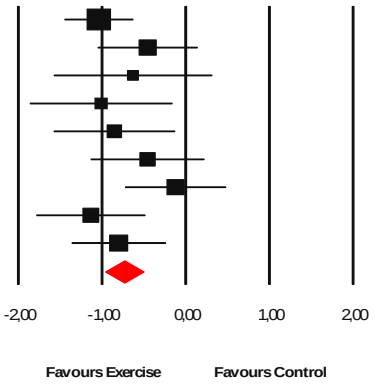
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
George 2011	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Pilu 2007	-1,04	0,40	0,16	-1,82	-0,25	-2,60	0,01
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Sadeghi 2016a	-0,85	0,37	0,14	-1,58	-0,12	-2,29	0,02
Sadeghi 2016b	-0,46	0,35	0,12	-1,14	0,23	-1,31	0,19
Veale 1992	-0,74	0,26	0,07	-1,25	-0,24	-2,89	0,00
	-0,92	0,11	0,01	-1,14	-0,70	-8,29	0,00



Meta Analysis

Aerobic Exercise in trials implemented from 2012 onwards

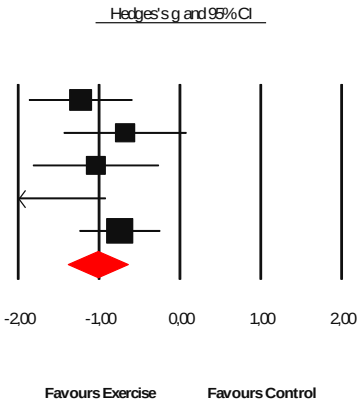
Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
George 2012	-1,04	0,21	0,04	-1,45	-0,62	-4,91	0,00
Kerling 2015	-0,45	0,31	0,09	-1,06	0,15	-1,48	0,14
Knochel 2014	-0,63	0,49	0,24	-1,58	0,32	-1,30	0,19
Legrand 2016	-1,01	0,44	0,19	-1,87	-0,15	-2,31	0,02
Sadeghi 2016a	-0,85	0,37	0,14	-1,58	-0,12	-2,29	0,02
Sadeghi 2016b	-0,46	0,35	0,12	-1,14	0,23	-1,31	0,19
Salehi 2016a	-0,12	0,31	0,10	-0,73	0,49	-0,39	0,70
Salehi 2016b	-1,13	0,33	0,11	-1,79	-0,48	-3,38	0,00
Schuch 2014	-0,80	0,29	0,08	-1,37	-0,23	-2,76	0,01
	-0,74	0,12	0,01	-0,97	-0,51	-6,31	0,00



Meta Analysis

Aerobic Exercise in trials implemented before 2012

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Martinsen 1985	-1,23	0,33	0,11	-1,87	-0,58	-3,73	0,00
Mota-Perreira 2011	-0,68	0,39	0,15	-1,44	0,09	-1,74	0,08
Pilu 2007	-1,04	0,40	0,16	-1,82	-0,25	-2,60	0,01
Reuter 1980	-2,01	0,56	0,31	-3,11	-0,91	-3,59	0,00
Veale 1992	-0,74	0,26	0,07	-1,25	-0,24	-2,89	0,00
	-1,02	0,19	0,04	-1,39	-0,65	-5,40	0,00



Meta Analysis

Chapter 5. Study 4.

Motivating clinically depressed adult patients to physical activity. A self-determination theory approach with clinical perspectives

Abstract

This study examinedifself-determination theory (SDT) islinked withamelioration of depression and physical activity participation in adult depressed outpatients.Participants were adult patients (aged 18-65) with a clinical diagnosis of major depressive disorder who were referred to the study by mental health professionals at the Vyronas-Kaissariani Community Mental Health Centre, Athens(Greece).Two structural equation models were computed to examine if the SDT dentrites comprising the three basic psychological needs(competence, autonomy and relatedness) and autonomous (internal and identified regulators) and controlling behavioural regulators(external, and introjected regulators) show a predictive power of on (i) depression and (ii) physical activity participation.A total of 206 moderately depressed adult patients (aged 18-65) with a clinical diagnosis of major depressive disorder comprised the study sample. Psychological needs illustrated a significant predictive impact on depression relief as well as on physical activity participation. The fruitful mediating effects of autonomous behavioural regulation were overcome by psychological needs in both models. Controlling forms of behavioural regulation showed no effect. Finally, the physical activity predictive properties of psychological needswere poisoned by depression.This study has shown the important role of need satisfaction for exercise with respect to depression relief and physical activity participation. This is emphasised by the fact that the direct impact of need satisfaction overcame the mediating effects of autonomous forms of behavioural regulation. Noteworthy, controlling forms of autonomous regulation that are widely seen in routine practice dealing with physical activity/exercise on prescription or promotion were unrelated to depression and physical activity participation. Finally, depression appeared to be having a toxic effect on the physical activity predictive properties of need satisfaction indicating that fostering need satisfaction facilitation is a highly demanding and challenging task.

Introduction

Depression is a disabling and lethal disorder that is associated with severe human suffering. Also, depression is projected to be the leading cause of burden of disease in high-income countries by 2020, as the lifetime prevalence is reaching alarming rates (World Health

Organization, 2013). To this extent, depression has been ranked as a top treatment target, especially major depressive disorder, which is a quite prevalent disorder that is typically treated in primary care (Üstün, 2001).

Exercise is prescribed as a treatment modality to depressed patients due to established association with antidepressant effects (National Institute for Clinical Excellence [NICE], 2009). However, depressed patients show the top drop out rates from exercise on prescription programmes (Crone, Johnston, Gidlow et al., 2008), despite their favourable predisposition (Fleischmann, 2003; Sigurdsson, Ólafsdóttir and Gottfredsson, 2008) and high uptake rates (Crone, Johnston, Gidlow et al., 2008; Harrison, McNair and Dugdill, 2005) to exercise. Notwithstanding the involvement of various factors in the sedentary lifestyle of depressed people, these findings suggest weak theoretical grounds to effectively support the facilitation of basic psychological needs for physical activityin consideration of the obviously differenttypes of motivation across the various stages of the behaviour. The theoretical construction of basic psychological needs and the distinction between the different types of motivation towards physical activity is made by self-determination theory (SDT), a meta-theory of human motivation (Ryan and Deci, 2000).

In SDT, motivation to behaviour is described by the way it is regulated on a continuum from lack of motivation via extrinsic controlled regulation to intrinsic controlled regulation. Extrinsic regulation refers to controlled behaviours and it is based either on external motivation to gain rewards, fulfil commitments and avoid pressure, or on introjected motivation to feel relief from shame, self-criticism or guilt. The least extrinsic regulation deals with identified motivation to behaviour in order to achieve goals of personal value. Finally, intrinsic regulation involves internal motivation, which is the most autonomous type of motivation to behaviour on the basis of interest, pleasure, or for the shake of the activity itself. Intrinsic regulation develops when social agents satisfy the three basic psychological needs of competence, autonomy, and relatedness which refer, respectively, to the perception of performing the behaviour effectively, self-managed and with a sense of social belonging. In particular, the higher the needs satisfaction, the more likely the motivation is to be internally regulated and the more internally regulated, the stronger the motivation, and the more likely is engagement in the behaviour.

Intrinsically rather than extrinsically regulated exercise participation has shown encouraging evidence in primary care. In contrast to extrinsic regulation, it predicts exercise participation and is related with lower illness symptoms during exercise (Sørensen, 2006). Also, in contrast to extrinsic regulation, autonomous regulation (internal and identified

motivation indexed into one entity) is linked with positive rather negative mood, and with higher levels of physical activity (Vancampfort, Madou, Moens et al., 2015). In addition, the action or maintenance stages of exercise behaviour show higher levels of intrinsic regulation in comparison to behavioural stages where people have not intentions to get physical (preconteplation) or think about getting physical in the next six months (Vancampfort, Stubbs, Venigalla et al., 2015; Vancampfort, Moens, Madou et al., 2016). These encouraging findings, however, cannot be generalized in outpatients with major depressive disorder as they stem either from physically active outpatients of mixed diagnoses (Sørensen, 2006), or from small numbers of major depressed, sedentary or outpatient participants (Vancampfort, Stubbs, Venigalla et al., 2015; Vancampfort, Madou, Moens et al., 2015; Vancampfort, Moens, Madou et al., 2016). Moreover, the above researchers have not explored the interplay of psychological needs satisfaction with behavioural regulation in relationship to depressionand to various levels of or intentions to physical activity participation.

Therefore, this study set to investigate if the SDT modelling involving psychological needs and behavioural regulationis able of depicting beneficial predictive properties towards affective constructs and behavioral patters, specifically, towards depression amelioration and physical activity participation. Also, the study examined for potential adverse effects of depression on the SDT modelling in relationship to physical activity.

Method

Participants

Participants were recruited at the Vyronas-Kesariani Community Mental Health Centre (VKCMHC) that supports the primary mental health care services of the Vyron and Kaisariani suburbs of the metropolitan City of Athens-Greece with approximately 90.000 inhabitants. Inclusion criteria referred to i) adult outpatients 18-65 years old, and ii) diagnosis of major depressive disorder by a VKCMHC psychiatrist or psychologist (responsible for their treatment) based on the Diagnostic and Statistical Manual (DSM-V) of the American Psychiatric Association (American Psychiatric Association, 2013). Patients were excluded from participation in case of a history of alcohol, substance or sexual abuse, manic or hypomanic episodes, or a diagnosis of depression resulting from bereavement, a medical condition (e.g., pregnancy), or from a physical or other mental disorder.

Recruitment was conducted through referrals by the VKCMHC staff for 29 consecutive months (from February 2014 to July 2016) in accordance to Helsinki designation and was co-ordinated by the author in collaboration withmental health professionals of the

VKCMHC. All participants read and signed an informed consent form approved by the University Ethics Committee prior to participating in the study. Data were collected and extracted by the author.

Outcome measures

Demographics

All participants read and signed an informed consent form approved by the University Ethics Committee prior to participation in the study. A series of sample characteristics were recorded through a self-report demographic list including gender, age, body mass index, and educational, marital, and smoking status.

Beck Depression Inventory (BDI)

The Beck Depression Inventory is a widely used self-rated measure of the severity of depressive symptoms in the last two weeks (Beck, Ward, Mendelson et al., 1961). The 21 items are organised in accordance to severity on a 4-point scale ranging from 0 to 3 and are summed from 0 to 63, with higher scoring indicating greater severity in depression. The BDI contains both cognitive and physical subscales (e.g., pessimism, worthlessness, fatigue and loss of energy) and includes items that refer to suicidal ideation. Cutoff points include: 0-14, minimal depression (0-9, remission from depression); 14-19, mild depression; 20-28, moderate depression; 29-63, severe depression. The instrument has been shown to be one of the most reliable and valid measures of depression, including in Greek patients (Lykouras, Oulis, Adrachta et al., 1998).In this study, the BDI showed good internal consistency (Cronbach alpha=0.89).

IPAQ-short form

IPAQ-short form is standardized instrument that measures physical activity through seven item that refer to the last seven days(Craig, Marshall, Sjöström et al., 2003). IPAQ-short formprovides physical activity quantification for the last seven days through four categories including vigorous intensity, moderate intensity, walking and sitting. IPAQ-short formhas shown satisfactory reliability and validity properties in the Greek population (Papathanasiou, Georgoudis, Papandreou et al., 2009).

Stage of Change

Stage of Change Theory (SOCT)(Prochaska and Diclemente, 1983)is a scale that comprises five potential stages towards physical activity participation for one hour five times per week. The five stages refer to precontemplation (do not think to become physically active), contemplation (intent to become physically active in the next six months), preparation (intent to become physically active in the immediate future), action (have started physical activity participation in the past six months) and maintenance (have sustained physical activity participation in the last six months).

Behavioural Regulation in Exercise

Participants' motivation for engaging in exercise was measured using the Behavioural Regulation in Exercise Questionnaire-2(BREQ-2; Markland and Tobin, 2004)(Moustaka, Vlachopoulos, Vazou et al., 2010). Participants were requested to respond to the BREQ-2 in terms of their reasons for exercising or wanting to engage in exercise. The BREQ-2 measures four different exercise regulations (i.e. intrinsic, identified, introjected and external). Each subscale was measured with four items except the introjected subscale, which comprised three items. An example item for intrinsic regulations is, 'I engage in physical activity because it is fun'; identified 'I value the benefits of physical activity'; introjected 'I feel very guilty when I don't exercise'; external 'I regularly engage in physical activity because other people say that I should' and amotivation 'I don't see the point in being physically active'. All items are scored between 0 (not at all true) and 4 (very true).

Psychological Needs in Exercise

The Basic Psychological Needs in Exercise Scale (BPNES) (Vlachopoulos and Michailidou, 2006)was used to assess the degree to which the basic psychological needs for autonomy, competence, and relatedness are fulfilled during exercise. The BPNES comprises 12 items (4 per subscale). Items follow the stem "In the present exercise setting . . ." and include for autonomy: "The exercise program I follow is highly compatible with my choices and interests," for competence: "I feel I have been making a huge progress with regard to the end result I pursue," and for relatedness: "I feel that I associate with the other exercise participants in a very friendly way." Participants were asked to report their agreement with the 12 statements by providing their responses on a 5-point Likert-type scale ranging from 1 (do not agree at all) to 5 (very strongly agree).

Data Analysis

Structural models were examined to test the hypothesized relationships. In these models, composite variables were used to represent the different subscales. The need satisfaction for competence, relatedness, and autonomy formed a latent factor reflecting need satisfaction. Intrinsic motivation and identified regulation formed a latent factor reflecting autonomous motivation; external and introjected regulation formed a latent factor reflecting controlled motivation. Three structural models were examined to test the hypothesized mediation for depression. First, a non-mediated direct model was tested, in which need satisfaction was hypothesized to predict depression. Second, a fully mediated model was tested, in which need satisfaction was hypothesized to predict motivational regulations (autonomous and controlled motivation), which in turn were hypothesized to predict depression. Third, a partially mediated model was tested, in which the direct paths from need satisfaction to stage of change was added, to test changes in the indirect effects (from need satisfaction to depression) in the presence of the direct effects.

Similarly, three structural models were examined to test the hypothesized mediation for stages of change. First, a non-mediated direct model was tested, in which need satisfaction was hypothesized to predict stage of change. Second, a fully mediated model was tested, in which need satisfaction was hypothesized to predict motivational regulations (autonomous and controlled motivation), which in turn were hypothesized to predict stage of change. Third, a partially mediated model was tested, in which the direct paths from need satisfaction to stage of change was added, to test changes in the indirect effects (from need satisfaction to stage of change) in the presence of the direct effects. Two additional models were tested to further explore the relationship of motivation with self-reported physical activity and depression. First, a model where stages of change were hypothesized to predict metabolic equivalent of task (METS) as these expressed through self-reported physical activity, and second a model where depression was added as an independent variable to explore which level of the motivational sequence was linked to depression.

Results

From a total of 257 patients identified as eligible for participation, 236 adult outpatients (92%) expressed an initial interest in participating in the study. A small number of the 236 patients, specifically 19 patients (8%) did not eventually participate in the study due to change of mind. Also, 10 patients (4%) did not attend the scheduled session due to change of mind or due to reasons irrelevant to the study (6 and 4 patients, respectively). Finally, one

patient did not complete the battery of outcome measures. To this extent, 206 patients (80% of the original sample) completed the battery of qiestionnaires and were included in the analysis.Demographicinformation of participants is presented in Table 1.

Table 1. Demographic information of the sample

	N; %	Age	
Total group	206; -	Mean= 45.89	SD= 12.37
Females	162; 78.60%		
Males	44; 21.40%		
Marital Status			
Single	15; 7.30%		
Engaged	1; 0.50%		
Affair	5; 2.40%		
Living together	8; 3.90%		
Divorced	50; 22.30%		
Married	81; 39.30		
Not Married	28; 13.60%		
Windowed	8; 3.90%		
Not reported	10; 4.90		
Education			
Students	8; 4.00%		
Tertiary	70; 34.00%		
Secondary	106; 51.50%		
Primary	22; 10.50%		
Job status			
Yes	70; 34.00%		
No	105; 51%		
Retired	31; 15.00%		
Non-Smokers	66; 32.00%		
Smokers	102; 49.50%		
Ex Smokers	28; 13.60%		
Not reported	10; 4.90%		
	Mean	SD	
Cigarettes per day	17.51	11.06	
Cigarettes previous day	16.22	11.39	

N= Number; SD=Standard Deviation

Examination of Cronbach's alpha showed acceptable internal consistency for all measures (Cronbach's alpha ranging from .67 to .90). In general, participants had moderate

scored in depression. They also scored moderately to high in the need satisfaction subscales and the autonomous motivation subscales, and low to moderately in the controlled motivation subscales. Finally, they scored low to moderately in stages of change. Descriptive statistics of the outcome measures are presented in Table 2.

Table 2. Descriptive statistics of outcome measures

Patients (N=206)	Cronbach Alpha	Mean	SD
BDI	.89	21.32	10.90
Amotivation	.75	0.63	0.65
External Regulation	.74	1.15	0.89
Introjected Regulation	.81	1.57	1.12
Identified Regulation	.67	2.64	0.82
Internal Regulation	.87	2.75	0.96
Competence	.94	3.71	1.90
Autonomy	.84	4.52	1.51
Relatedness	.89	4.53	1.70
Body Mass Index		26.04	5.58
IPAQ 1 days vigorous		.29	.896
IPAQ 2 min vigorous		61.88	33.91
IPAQ METS vigorous		141.74	551.10
IPAQ 3 days moderate		.77	1.58
IPAQ 4 min moderate		52.40	22.76
IPAQ METS moderate		157.66	349.54
IPAQ 5 days walking		5.67	1.923
IPAQ 6 min walking		66.75	87.34
METS WALK		1341.69	1915.00
IPAQ 7sedentary time		359.22	222.75
METS TOTAL		1641.10	2010.11

BDI: Beck Depression Inventory; IPAQ: Internal Physical Activity Questionnaire; METS: Metabolic Equivalents

Preliminary analyses

Correlations were calculated between psychological need satisfaction and motivational regulation (Table 3). Subsequently, two one-way MANOVA was calculated to test for differences in psychological need satisfaction and motivational regulation. Regarding need satisfaction the analysis revealed a significant multivariate effect, $F (4, 199) = 6.55$, $p < .01$. Examination of the univariate statistics showed significant differences for competence, $F (4, 199) = 19.95$, $p < .01$, and relatedness $F (4, 199) = 4.82$, $p < .01$. Regarding motivational regulation the analysis showed a significant multivariate effect, $F (5, 198) = 6.88$, $p < .01$. Examination of the univariate statistics showed significant differences for identified

regulation, F (4, 199) = 7.95, p < .01, and intrinsic motivation F (4, 199) = 3.79, p < .01. Mean scores and group comparisons are presented in Table 4.

Participants were grouped into exercisers and non-exercisers based on their responses on the IPAQ. Individuals reporting any frequency of moderate or vigorous exercise were classified as exercisers; the rest of participants were classified as non-exercisers. A total of 67 participants were identified as exercisers, whereas 139 were identified as non-exercisers.

Subsequently, analyses of variance were conducted to compare the two groups on depression, need satisfaction, motivational regulation, and stage of change. Regarding depression, t-test revealed a significant effect, $t(204) = 4.31$, $p < .01$, with exercisers showing lower depression than non-exercisers. Regarding need satisfaction, one way-MAVOVA showed a significant effect, $F(3, 202) = 19.15$, $p < .01$, partial $\eta^2 = .22$. Examination of the univariate tests showed that exercisers scored higher than non-exercisers on the need for competence, $F(1, 205) = 53.15$, $p < .01$, partial $\eta^2 = .21$, and the need for autonomy, $F(1, 205) = 7.90$, $p < .05$, partial $\eta^2 = .04$, whereas no differences were found for the need for relatedness, $F(1, 205) = 0.07$, $p = .80$. Regarding motivational regulation, one-way MANOVA showed a significant effect, $F(4, 201) = 2.90$, $p < .01$, partial $\eta^2 = .06$. Examination of the univariate tests showed that exercisers scored higher than non-exercisers on intrinsic motivation, $F(1, 205) = 5.30$, $p < .05$, partial $\eta^2 = .03$, and identified regulation, $F(1, 205) = 10.66$, $p < .01$, partial $\eta^2 = .05$, whereas no significant differences were identified for introjected regulation, $F(1, 205) = 0.00$, $p = .99$, and extrinsic motivation, $F(1, 205) = 0.07$, $p = .78$. Regarding stage of change, t-test revealed a significant effect $t(202) = 7.93$, $p < .01$, with exercisers reporting more advanced stages than non-exercisers.

TABLE 3. Correlations between psychological needs and motivatinal regulation

Variables	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*
Psychological needs								
1. Competence								
2. Autonomy	.32**							
3. Relatedness	.25**	.28**						
Bevavioral regulators								
4. Identified	.46**	.15*	.09					
5. Internal	.36**	.15*	.16*	.56**				
6. Introjected	.09	.05	-.11	.35**	-.06			
7. External	-.04	-.05	.03	.07	-.07	.40**		
8. Amotivation	-.30**	-.05	-.00	-.41**	-.37*	-.10	.13	

*significant at 0.05; **significant at 0.01

TABLE 4. Descriptive statistics for Psychological Needs and Motivational Regulation as a function of Stage of Change

Patients (N=206)	***1.*** Pre-conteplation (N=64)	***2.*** Conteplation (N=37)	***3.*** Preparation (N=38)	***4.*** Action (N=24)	***5.*** Maintenance (N=41)
Competence					
M (SD)	2.97 (1.86)	3.52 (1.77)	3.82 (1.67)	4.28 (1.55)	4.63 (2.01)
	1<3,4,5	2<5•	3>1, 3<5	4>1	5>1,2,3
Autonomy					
M (SD)	4.32 (1.65)	4.22 (1.46)	4.74 (1.54)	4.72 (1.09)	4.86 (1.49)
		2<5			5>2•
Relatedness					
M (SD)	4.09 (1.84)	4.71 (1.58)	5.21 (1.47)	3.76 (1.51)	4.94 (1.58)
	1<3,5	2>4	3>1, 4	4<2, 3, 5	5>1, 4
Amotivation					
M (SD)	0.77 (0.71)	0.53 (0.52)	0.59 (0.69)	0.54 (0.52)	0.60 (0.70)
External					
M (SD)	1.22 (0.92)	1.27 (0.88)	1.21 (1.02)	0.96 (0.71)	0.98 (0.83)
Introjected					
M (SD)	1.36 (1.08)	1.79 (1.10)	1.82 (1.22)	1.63 (1.14)	1.38 (1.08)
	1<2•	2>1•	3>1		
Identified					
M (SD)	2.24 (0.91)	2.66 (0.55)	3.08 (0.58)	2.68 (0.67)	2.80 (0.89)
	1<2, 3, 4, 5	2>1, 2<3	3>1, 3>2, 3>4	4>1, 4<3	5>1
Internal					
M (SD)	2.46 (1.09)	2.61 (0.88)	3.01 (0.97)	2.68 (0.74)	3.09 (0.79)
	1<3, 1<5	2<3•, 2<5,	3>1, 3>2•		5>1, 5>2

M=Mean; SD=Standard Deviation; All findings are statistically significant at 0.05; •Findings with p values at 0.06

Structural models

SDT and Depression

A direct structural model was tested to investigate the degree to which need satisfaction would predict depression. The analysis revealed a perfect fit for the hypothesized model (CFI = 1.00, RMSEA = .01). Need satisfaction negatively predicted depression explaining 18% of the total variance. The direct structural model is presented in Figure 1.

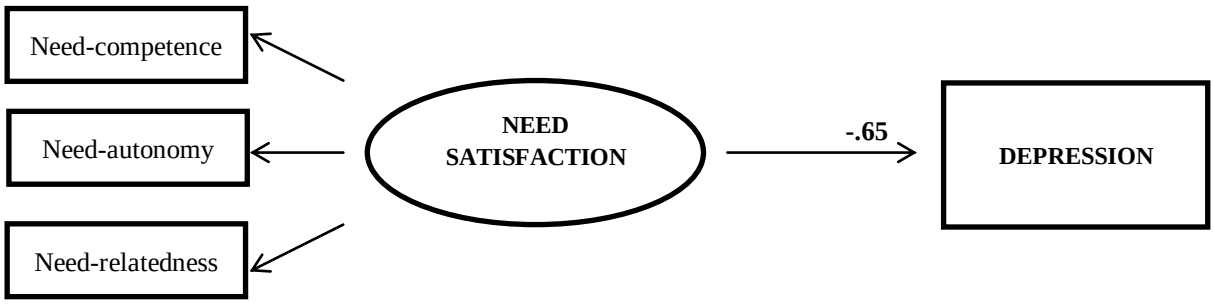


Figure 1.

Subsequently, a fully mediated model was tested to investigate if motivational regulations would mediate the relationships between need satisfaction and depression. The analysis revealed an acceptable fit for the hypothesized model (CFI = .96, RMSEA = .11). Need satisfaction positively predicted autonomous motivation, which in turn negatively predicted depression; the relationship between need satisfaction and controlled motivation was very low, negative, and non-significant, whereas the relationship between controlled motivation and depression was low, positive and non-significant. The indirect effect from need satisfaction to depression through autonomous motivation was negative and significant (standardized coefficient: .27). Overall, the model explained 15% of the total variance. The fully mediated structural model is presented in Figure 2.

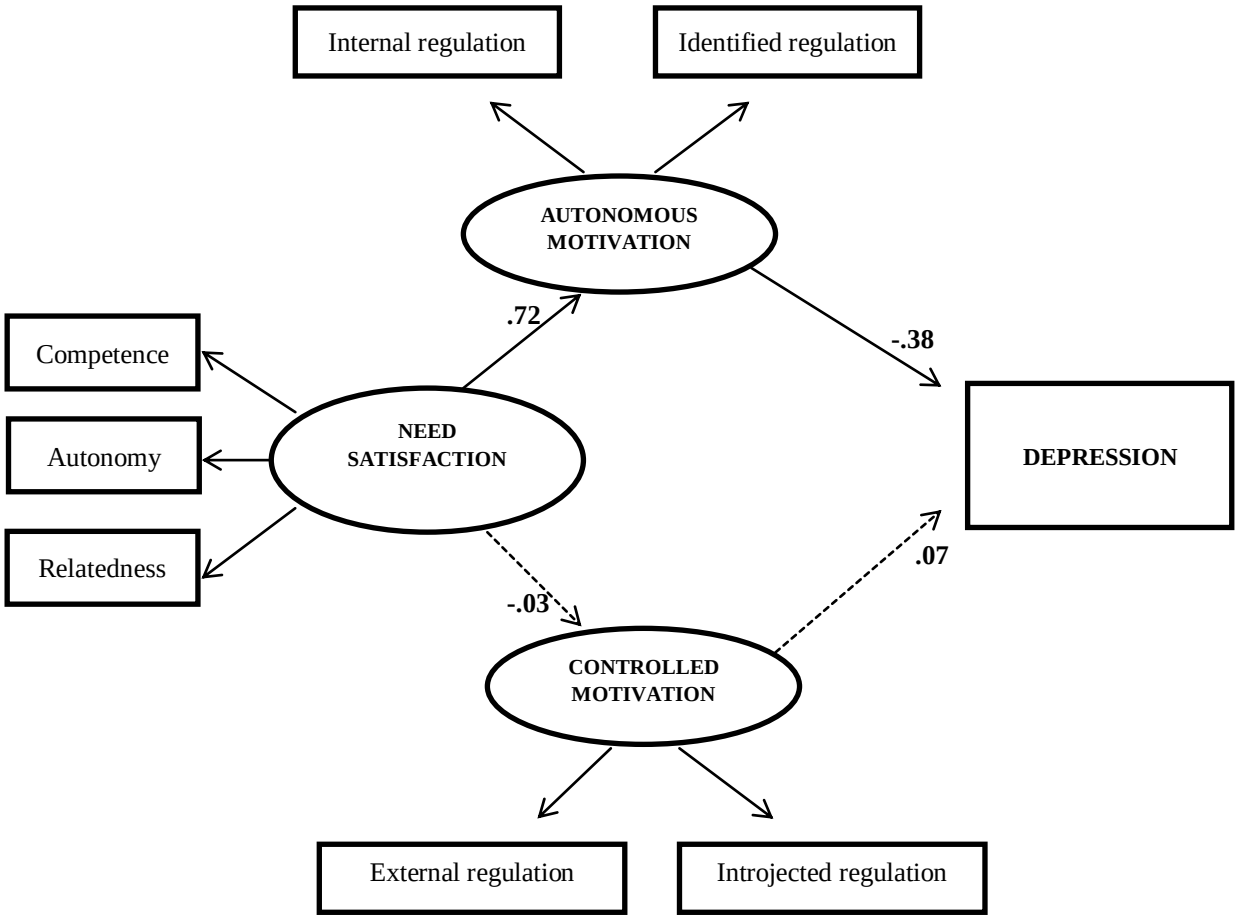


Figure 2. Dashed lines indicate non-significant relationships

Finally, a partially mediated model was tested, where the direct path from need satisfaction to depression was added. The analysis revealed a good fit for the hypothesized model (CFI = .99, RMSEA = .07). The results showed that the direct path from need satisfaction to depression was negative and significant, whereas the effect from autonomous motivation to depressionbecamepositive and non-significant, and the indirect effect from need satisfaction to depression became positive and non-significant. The results suggest that the direct effect from need satisfaction to depression outweighed the indirect effect through autonomous motivation. The model explained 42% of the total variance. The partially mediated model is presented in figure 3.

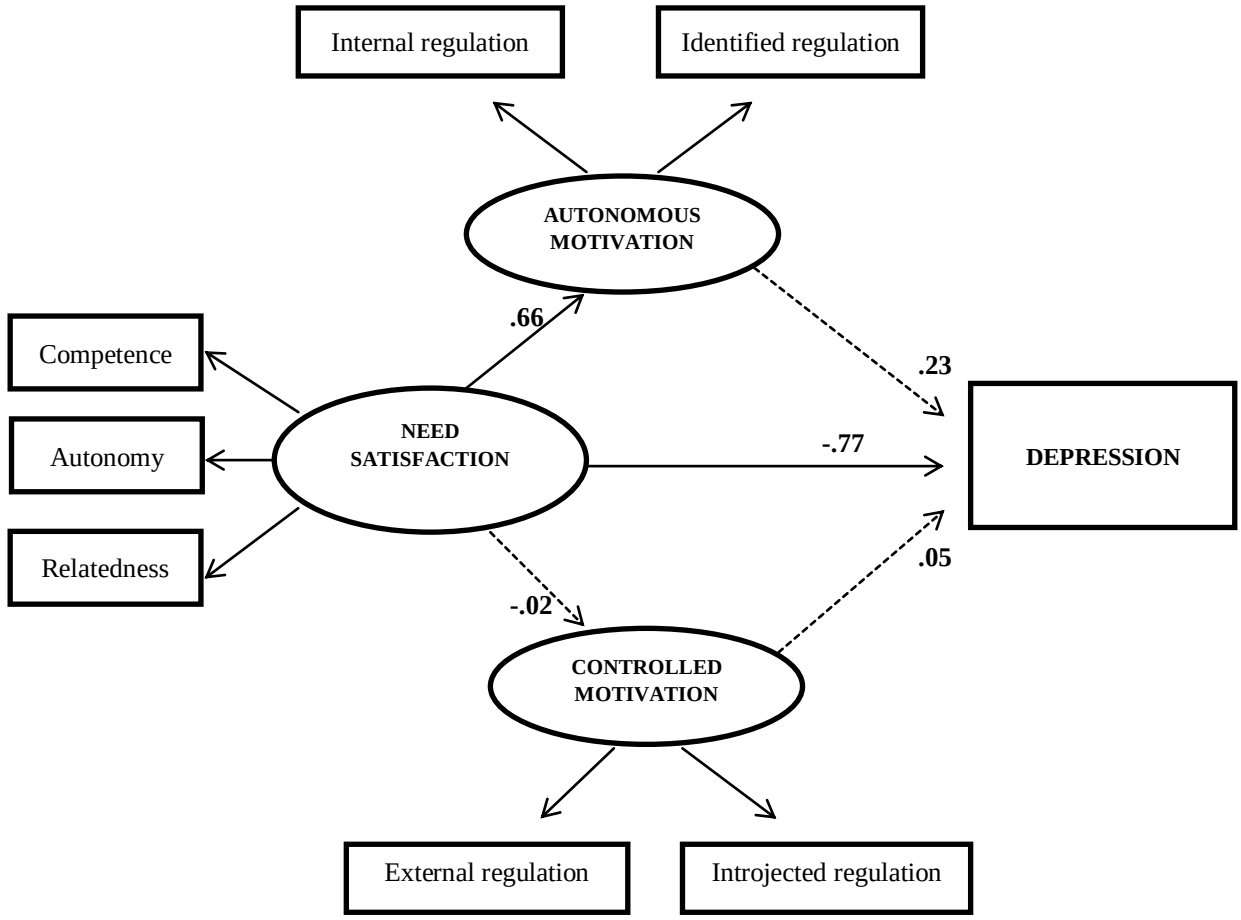


Figure 3. Dashed lines indicate non-significant relationships

SDT and physical activity

A direct structural model was tested to investigate the degree to which need satisfaction would predict stage of change. The analysis revealed an acceptable fit for the hypothesized model (CFI = .95, RMSEA = .08). Need satisfaction positively predicted stage of change explaining 18% of the total variance. The direct structural model is presented in Figure 4.

Figure 4.

Subsequently, a fully mediated model was tested to investigate if motivational regulations would mediate the relationships between need satisfaction and stage of change. The analysis revealed an acceptable fit for the hypothesized model (CFI = .99, RMSEA = .07). Need satisfaction positively predicted autonomous motivation, which in turn positively predicted stage of change; the relationship between need satisfaction and controlled motivation was very low, negative, and non-significant, whereas the relationship between controlled motivation and stage of change was low, negative and non-significant. The indirect effect from need satisfaction to stage of change through autonomous motivation was positive and significant (standardized coefficient: .24). Overall, the model explained 15% of the total variance. The fully mediated structural model is presented in Figure 5.

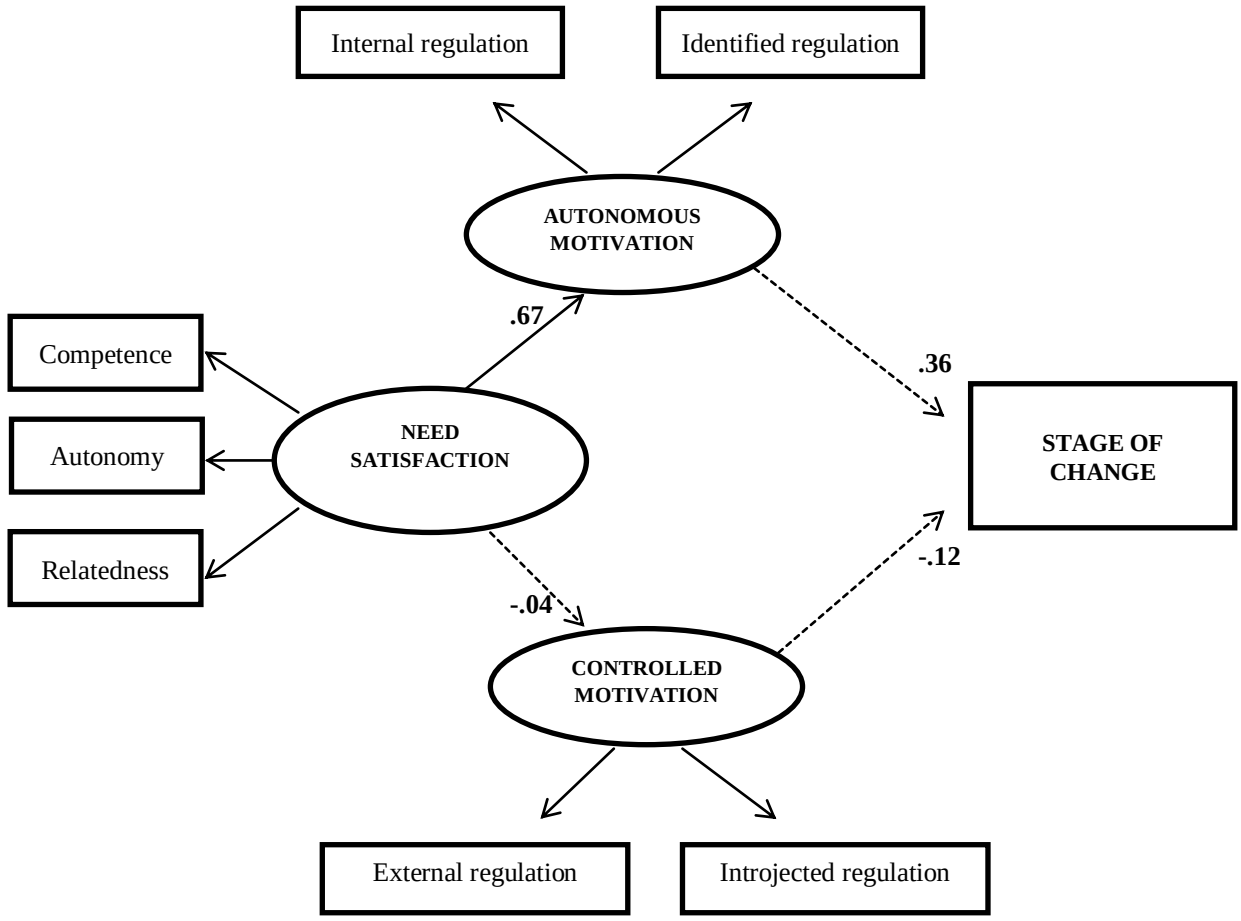


Figure 5. Dashed lines indicate non-significant relationships

Finally, a partially mediated model was tested, where the direct path from need satisfaction to stage of change was added. The analysis revealed an acceptable fit for the hypothesized model (CFI = .99, RMSEA = .06). The results showed that the direct path from need satisfaction to stage of change was significant, whereas the effect from autonomous

motivation to stage of change, and thus also the indirect effect from need satisfaction to stage of change, became non-significant. The results suggest that the direct effect from need satisfaction to stage to change outweighed the indirect effect through autonomous motivation. The model explained 18% of the variance. The partially mediated model is seen in figure 6.

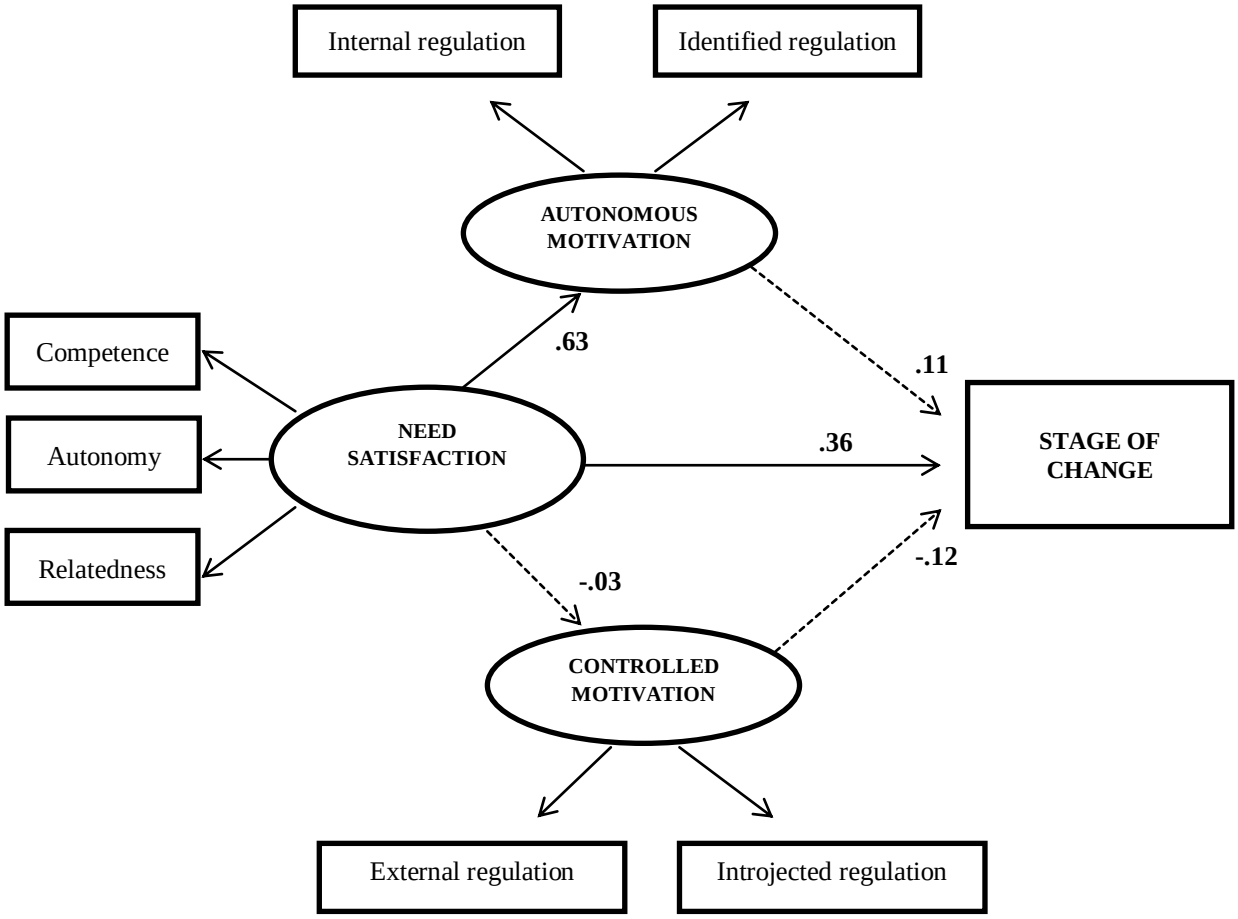


Figure 6. Dashed lines indicate non-significant relationships

In the following model the METs were added to test the degree to which the motivational model could predict self-reported physical activity. The analysis revealed an acceptable fit for the hypothesized model (CFI = .93, RMSEA = .04). The results showed that the direct path from stage of change to METS was positive and significant. In addition, the indirect path from need satisfaction to METS was positive and significant (standardized coefficient: .14). The model explained 16.5% of the total variance. The model including physical activity is presented in figure 7.

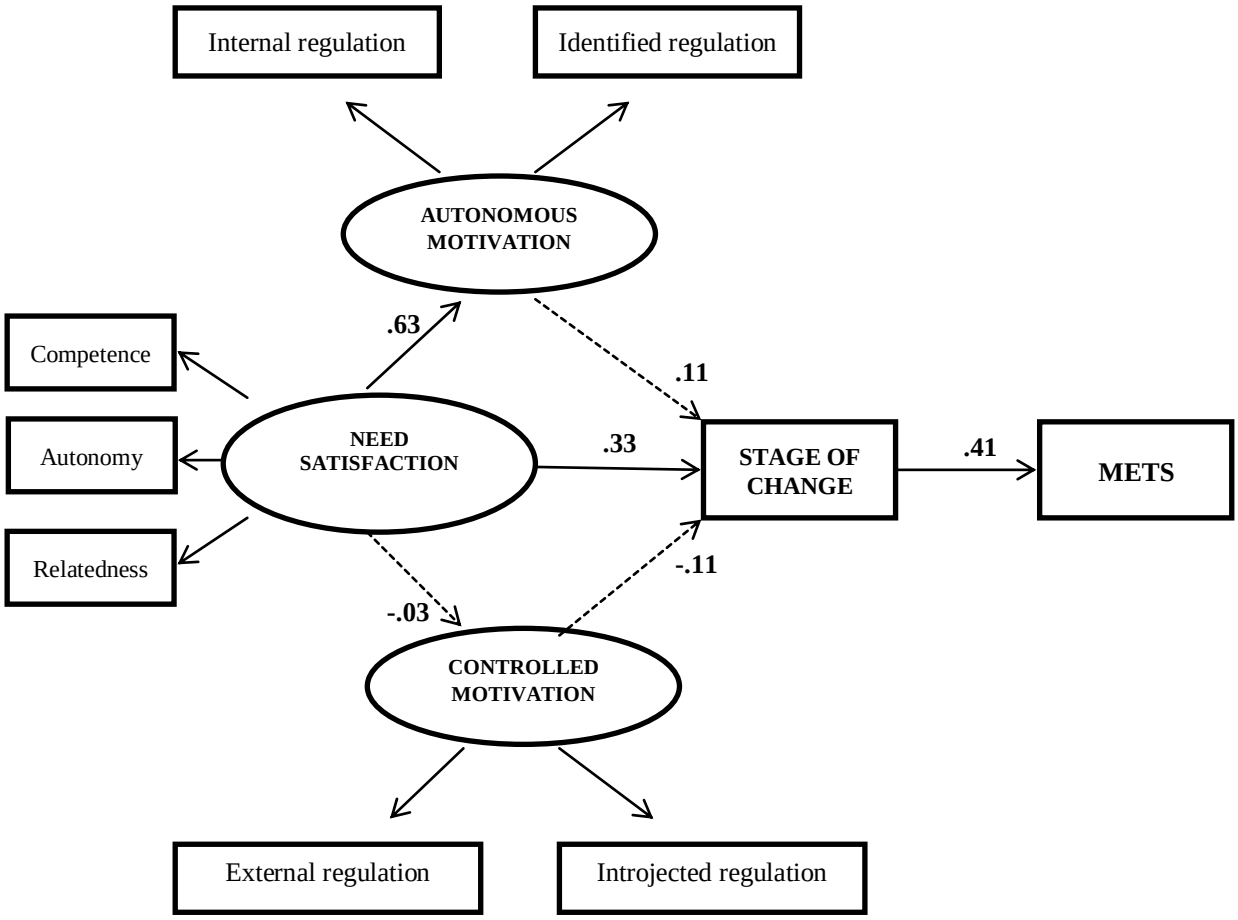


Figure 7. Dashed lines indicate non-significant relationships

Also, depression was added to the model. Direct paths were added from depression to need satisfaction, autonomous and controlled motivation, and stage of change to explore what aspects of the motivational process depression are associated with. The analysis revealed an acceptable fit for the hypothesized model (CFI = .93, RMSEA = .05). Depression was negatively related only with need satisfaction predicting 38% of the total variance. The model including depression is presented in Figure 8.

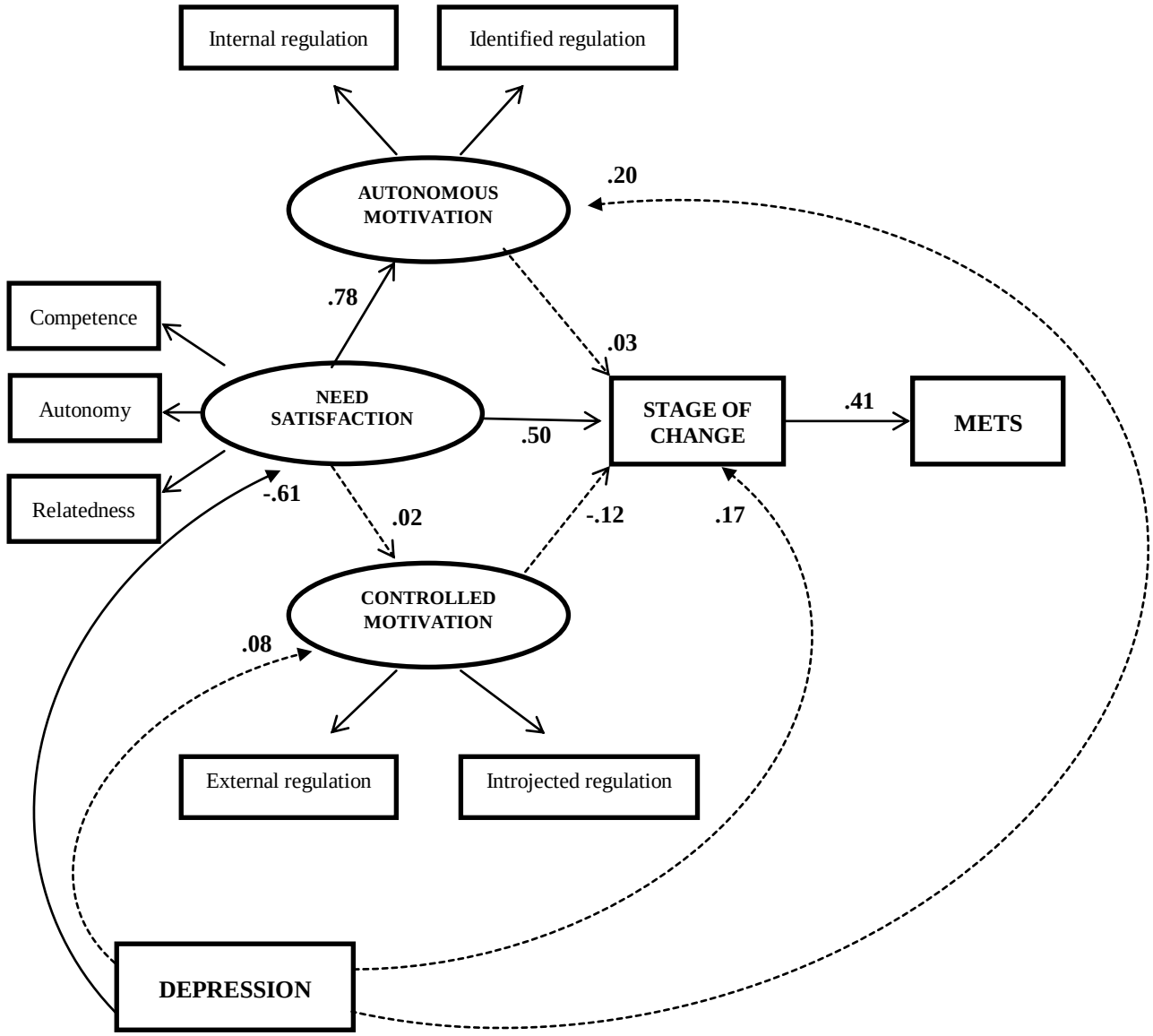


Figure 8. Dashed lines indicate non-significant relationships

Discussion

The present study aimed at testing SDT in relationship todepression and physical activity in depressed adults. In particular, the study (a) examined the relationship between the satisfaction of psychological needs in exercise and depression, and the potentially mediating role of behavioural regulation in this relationship; and (b) the relationships between the satisfaction of psychological needs and stages of change and the potentially mediating role of behavioural regulation in this relationship; in addition, the strength of the model in predicting self-reported physical activity was tested; and finally, aiming at exploring at which stage of the motivational process depression may have a deleterious effect, depression was also tested as an independent, to the motivational sequence, variable. Overall, the results have provided

interesting insights regarding the links between SDT tenets and depression, but also SDT tenets and physical activity in adult patients with major depressive disorder.

SDT and depression

The inverse prediction of depression by the psychological needs (figure 1) of competence, autonomy, and relatedness is in alignment with the SDT premises and the profile of depression. Particularly, depressed patients show low perceived and actual physical competence (Van de Vliet, Van Coppenolle and Knapen, 1999; Van de Vliet, Knapen, Onghena et al., 2002), absence of positive autonomous experiences due to poor self-management of various situations in daily life (Simmons and Kritchevsky, 1993) and increased social isolation (American Psychiatric Association, 2013)whereas SDT reports the predictive impact of psychological needs on depression (Ryan and Deci, 2000). Thus, fostering needs satisfaction for exercise is a reasonably SDT contributor to the amelioration of depression.

Further (figure 2), when autonomous and controlling behavioural regulators were tested for mediating effects on the contribution of need satisfaction to depression relief, the emerged grid pointed that psychological needs were linked only, and in a positive manner, with autonomous behavioural regulators. Also, autonomous behavioural regulators predicted depression amelioration. Accordingly, need satisfaction predicted indirectly depression relief through autonomous behavioural regulators. In contrast, need satisfaction was not related with controlling behavioural regulators, and controlling behavioural regulators in return were not linked with depression. In the subsequent model (figure 3), when a direct path from needs satisfaction to depression was added, the relationship between autonomous regulation and depression became non-significant, showing that need satisfaction predicted directly depression, without the mediation of behavioural regulation. Hence, the satisfaction of basic psychological needs showed robust antidepressant predictive properties by their own right.

The lack of any significant mediating role for behavioural regulation, and in particular autonomous regulation, should be interpreted in light of the fact that almost seven out of the ten participants (67%) were physically inactive. It is thus reasonable to speculate that sedentary depressed patients are, in line to their nosological profile, occupied by a pessimistic state including lack of pleasure, interest and personal value towards health behavioural patterns such as physical activity.Hence advanced need satisfaction for exercise is seen as the essential preceding step towards depression relief.

It should also be noted that controlling behavioural regulators manifested no significant relationship in any of the above models. This finding formulates suggestive grounds for considering that exercise regulation by external or introjected types of extrinsic motivation that deal with external gains or self-blame is dissociated with need satisfaction and with changes in depression. Accordingly, the typical iatrogenic approach to physical activity/exercise on prescription or promotion that is based on health-oriented consultancy putting an emphasis on health gains was unsupported by the current finding. Instead, a collective interpretation of the current findings suggests consultancy sessions could consider that solely satisfying the psychological needs of competence, autonomy and relatedness for exercise will contribute to the explanation of depression amelioration.

SDT and physical Activity

Need satisfaction predicted physical activity explaining 18% of the total variance (figure 4) whereas autonomous but not controlled behavioural regulators mirrored a supportive mediation on this link; need satisfaction predicted autonomous regulators, which in turn, they interacted positively with physical activity. Also, the indirect need satisfaction impact on physical activity through autonomous regulators remained positive and significant. The contribution of autonomous behavioural regulators to the explanation of the total variance amounted to 15% (figure 5). Testing, however, the direct effect of need satisfaction, the study found a predictive and prevailing path to physical activity, given that the autonomous behavioural regulation effect on physical activity as well as the indirect need satisfaction effect (through autonomous regulators) on physical activity became non-significant. This relationship accounted for 18% of the total variance (figure 6).

Accordingly, psychological needs emerged as the leading contributor towards participation in physical activity given that their direct predictive impact prevailed and neutralized the mediation of autonomous regulators. It is, therefore, critical to consider the satisfaction of psychological needs of competence, autonomy and relatedness for physical activity participation. While relevant SDT-based suggestions have been formulated in a recent critical review for exercise in major depressed patients (Morres, Stathi, Martinsen et al., 2014), it should be highlighted that SDT posits the synergetic (Deci, Eghrari, Patrick et al., 1994) and cautious (Ryan and Deci, 2017)facilitation of the satisfaction of the three basic psychological needs. Relevant details can be found in the critical review by Morres, Stathi, Martinsen et al. (2014).

Indeed, satisfacting the psychological needs of competence, autonomy and relatedness mayplay an important role for implementing physical activity programs for depressed patients. Particularly, Bodin and Martinsen (2004) found that exercise participation linked with increased performance confidence has more beneficial mental health effects in comparison to exercise participation where performance confidence showed no positive changes. Also, Callaghan, Khalil, Morres et al. (2011) found that autonomous-based exercising, such as preferred intensity exercise, was related with higher relief in depression compared to less autonomous exercising such as prescribed (fixed intensity) exrcising. Finally, Wormald and Ingle (2004) have highlighted thecorrelationof relatedness with physical activity given that relatedness (i) was expressed as an outcome expectation by prospective exercisers and (ii) interplays with dropouts whenunfulfilled.

In the subsequent model (figure 7), stage of change predicted higher self-reported Metabolic Equivalents (METS) of physical activity whereas need satisfaction documented a significantly positive indirect path to METS. Based on these findings, self-reported physical activity was positively linked to corresponding self-reported energy expenditure. This indicates an encouraging consistency in the cohesion of the findings given the positive predictive sequence from various levels of physical activity to the associated energy expenditure. It is also, important to underline the predictive power of psychological needs attributable to their mediating effect on the above predictive sequence. Overall, need satisfaction in this study emerged as the key SDT factor in the prediction of physical activity participation.

Also, depression was included in the above grid to inform whether direct predictive paths could be recorded. Depression had no predictive effect on motivation processes (autonomous or controlling behavioural regulators) or on the stage of change. However, depression detected a negative effect on psychological needs showing a large deconstructive influence as this model accounted for 38% of the total variance (figure 8). The toxic effect of depression on need satisfaction portrays the necessity to take into consideration the great importance of fostering need satisfaction, especially since need satisfaction emerged as the global trigger for the prediction of physical activity in depressed patients

Conclusions

This study was the first to examine the SDT properties in relation to depression and physical activity in a sample of adult outpatients with major depressive disorder. This sample was predominantly sedentary. Psychological needs emerged as the most important SDT factor

attributable to their leading and direct role in predicting depression relief or physical activity participation. However, depression appeared, in addition, to be carrying adverse effects on need satisfaction. Notwithstanding the inability to provide any prospective or causal outline due to the non-longitudinal design of the study, some important recommendations have emerged. Given that the majority of the study participants were sedentary, it should be acknowledged that need satisfaction facilitation seems to be a preceding factor to physical activity participation. However, need satisfaction is infected by depression, a clear indication of the requirement to provide an increased and cautious fostering of need satisfaction. Finally, controlling forms of behavioural regulators representing the most widely used consultancy form in physical activity/exercise on prescription or promotion schemes showed no predictive effect on depression or on physical activity participation. Further research is needed to specify the most influential autonomous-, relatedness- and competence-supportive agents and components for exercise in sedentary adult outpatients with major depressive disorder, and help supporting causal inferences regarding the seemingly reciprocal relationship between depression and motivation.

Chapter 6. Study 5

Habitual physical activity and accelerometer devices in adult outpatients with major depressive disorder.

Abstract

The purpose of this cross sectional study was toexamine the association of objective measures of habitual physical activity levels with depression in outpatients with major depressive disorder aged 18-65 years. A total of 19 adult outpatients with major depressive (mean age=47.79 ±11.67) disorder participated in the study. Subjective measurements recorded depression, mood and quality of life. Objective measures included triaxial accelerometer devices that measured habitual physical activity for a period of one week.Regression analysis with a stepwise method was computed to examine the predictive properties of habitual physical activity on depression.Participants displayed a mild to moderate depression (mean=17.10 ± 8.70), wore the device for a mean of 6.26 ± 1.24 days,showed 7.545,02 ± 5.212,95 steps/day, and spent 515.33 ± 155.71 min/day in sedentary time and31.59 ± 25.83 min/day in moderate to vigorous PA (MVPA). Only 40seconds represented the vigorous part of the 31.59 minutes. Finally, the mean wear time per days with valid wear time was 13.40 ± 2.61 hours/day. Moderate to vigorous physical activity contributed to the prediction of depression (Beta = -.48, t = -2.25, $p < .05$). The model predicted 23% of the depression variance. Light physical activity showed no predictive properties on depression. Also, no significant correlations were found between mood and quality of life with objective levels of physical activity. Based on this study, major depressed adult outpatients accumulate 192 minutes of moderate to vigorous habitual physical activity per week and this ammout of time shows antidepressant predictive properties. To this extent, habitual physical activity seems to be a promising front-line antidepressant intervention.

Introduction

Although repeated evidence has related sedentary behaviourtoincreased risk of depression (Zhai, Zhang and Zhang, 2015) and physical activity to lower levels of depression (Harris, Cronkite and Moos, 2006), physical activity components integrated in daily life such as work- or house-related physical activities are not necessarily associated with lower mental health problems (White, Babic, Parker et al., 2017).This is a major issue in the treatment of depression asdepressed patientsare often advised to quite their sedentary lifestyle and to increase their physical activity levelseither through the path of physical activity/exercise on prescription schemes or through the path of the adoption of a physically active lifestyle. Given that the former pathis associated with disappointing dropout rates andpotential solutions have beensuggested in the previous chapter, it remains to be explored ifhabitual physical activity that is recommended by the World Health Organisation for acquiring health benefits(e.g., weekly dose of 150minutes of moderate intensity)(World Health Organization, 2011)is associated with depression relief in clinically depressed adult outpatients(18-65) receiving treatment for depression.

Therefore, it is necessary to record daily life physical activity levels by means of objective measures. Compared to self-report measures, objective measures include the advantage of ruling out potential confounding effects caused by social desirability or by cognitive dysfunction in recalling information.Over the last decades, accelerometers represent a valuable source of evidence for the objective levels of daily physical activity.In mental health patients, objective measures of physical activity are seen as an advantage given the significant differences in physical activity and sedentary behaviour levels between self-report and objective measures (Stubbs, Williams, Gaughran et al., 2016; Stubbs, Firth, Berry et al., 2016; Vancampfort, Firth, Schuch et al., 2016).Also, recent meta-analyticstudieshavefound that patients with major depressive disorder exhibit lower physical activity levels compared to healthy controls(Burton, McKinstry, Tătar et al., 2013; Schuch, Vancampfort, Firth et al., 2017), especially when objective measures physical activity levels are recorded(Schuch, Vancampfort, Firth et al., 2017).However, the association of objective levels of physical activity with depression in adult depressed outpatients aged 18-65 has been hardly examined.

Specifically, in a large study that was conducted in Sweden, Helgadóttir, Forsell and Ekblom (2015)found an inverse association between depression and objective physical activity levels,specifically, depression predicted lower levels of light physical activity but showed no relationship with moderate to vigorous physical activity.However, the large sample included patients with depression (12.9%), anxiety (13.5%) or concurrent depressive

and anxiety (73.6%) disorders and seemed to be motivated to exercise as the relevant recruitment was conducted in light of participation in an exercise programme that it was about to begin. In addition, a number of participants were recruited by media advertisements.

Also,Wielopolski, Reich, Clepce et al. (2015)conducted a small longitudinal study and revealed negative strong correlations between objective physical activity and depression. However, these findings were recorded within the context of an inpatient psychiatric unit and cannot be generalised for the treatment of depression due to a twofold reason: (i) the majority of depressed patients are treated in primary care(Pence, O'Donnell and Gaynes, 2012) and (ii) the inpatient milieu is entirely different compared to the daily living milieu. As Wielopolski, Reich, Clepce et al. (2015) reported, studies in outpatients with major depressive disorder are essential. To this extent, the current study aimed at exploringthe predictive effect objectively measured habitual physical activity on depression in clinically depressed adult outpatients.

Method

Participants

From January 2016 to June 2016, mental health professionals of the Vyronas-Kaissariani Mental Health Community Centreadministrated the process of recruiting depressed patients aged 18-65 years. A total of 32 adult patients with a DSM-IV diagnosis for major depressive disorder(American Psychiatric Association, 2000)were considered eligible for participation and were referred to the study; participants were explained about the purpose and involved requirements of the studyand the voluntarystatus of participation. Almost 70% of the sample (23 patients) expressed an initial interest in participating in the study and the researcher (the author) took up the follow-up. To this extent, appointments were set uptoprovidepatients with detailed information regarding the purpose of the study and the involved participation requirementsincluding completion of self-report questionnaires and accelerometer use instructions (explained below). All patients were informed in detail about the voluntary status of participation, the right to dropout of the programme any time they would decided, and the necessity to fill-out outcome measures upon the return of the accelerometer device, specifically upon the completion of the seventh day of accelerometer use. A total of 20 patients agreed to participate in the study and provided a signed informed consent. Then,accelerometers were calibrated andactivated for a 7-day use, and were delivered to participants. Finally, participants scheduled an appointment to return the accelerometer and to fill-out outcome measures upon the completion of the seventh day of accelerometer use.

All but two patients returned the accelerometer devices upon the scheduled appointment, and completedthe outcome measures (described below). The remaining two patients presented at the Centre within 24 hours after the scheduled appointment. Of the 20 patients, one female patient dropped out of the study due to change of mind and returned the accelerometer after ten days.To this extent,19 participants (13 females) provided the full set of data. The age range of the programme completers was 22 to 65 years (Mean 47.79± 11.67) with a Body Mass Index of 26.04 ± 5.69.All patients signed an informed consent prior to participation.

Objective outcome measures

Physical Activity

Participants were asked to wear a small (3.8cm × 3.7cm × 1.8cm), light (27 gr) accelerometer device (Actigraph GT3X+, Actigraph LLC, Pensacola, FL) on the right waist with an elastic belt for a period of seven consecutive days(Corder, Brage and Ekelund, 2007; Murphy, 2009). Also, participants were instructed to wear this motion sensor during all waking hours except when sleeping and bathing.An epoch length of 60 seconds was chosen to capturephysical activity (PA) and sedentary behavior. Freedson equation for adults(Freedson, Melanson and Sirard, 1998) was used to define physical activity cut points and to diagnose time spent in different physical activityintensities (Sedentary time: < 100 cnts·min^{-1}, Light PA/ LPA: 100 - 1951 cnts·min^{-1}, Moderate PA/ MPA: 1952 - 5724 cnts·min^{-1}, Vigorous PA/ VPA: 5725 – 9498 cnts·min^{-1}, Very Vigorous PA/ VVPA >= 9499 cnts·min^{-1}). Data were downloaded and analyzed with ActiLife software version 6.5.2.This study retained as valid data only the data that were downloaded from the participants who wore the device for at least three days of a minimum of 8 hours per day. Periods of more than 60 minutes of consecutive zero counts were considered non-wear time(Ward, Evenson, Vaughn et al., 2005).

Subjective outcome measures

Beck Depression Inventory (BDI)

The Beck Depression Inventory is a widely used self-rated measure of the severity of depressive symptoms in the last two weeks(Beck, Ward, Mendelson et al., 1961). The 21 items are organised in accordance to severity on a 4-point scale ranging from 0 to 3 and are summed from 0 to 63, with higher scoring indicating greater severity in depression. The BDI contains both cognitive and physical subscales (e.g., pessimism, worthlessness, fatigue and loss of energy) and includes items that refer to suicidal ideation. Cutoff points include: 0-14,

minimal depression (0-9, remission from depression); 14-19, mild depression; 20-28, moderate depression; 29-63, severe depression. The instrument has been shown to be one of the most reliable and valid measures of depression, including in Greek patients(Lykouras, Oulis, Adrachta et al., 1998). In this study, the BDI showed good internal consistency (Cronbach alpha=0.89).

The Four Dimensional Mood Scale (4DMS)

The Four Dimensional Mood Scale (4DMS) is a self-reported questionnaire consisted of 20 items rated at 5-point Likert scale that assess positive energy (4 items) negative arousal (6 items), relaxation (5 items), and tiredness (5 itmes).Internal consistency reliabilities range from .87 to .93(Huelsman, Richard C. Nemanick and Munz, 1998). In this study, reliability coefficients (Cronbach alpha) ranged from .89 to .92.

Quality of Life

The SF-12 Health Survey is a self-report questionnaire with items scoring on a Likert scale and high reliability coefficients(Ware Jr, Kosinski and Keller, 1996). It evaluates health-related quality aspects of life referred to physical and mental health. These include physical limitations, dysfunction due to physical health problems or due to emotional health problems, social functioning,emotional wellbeing, energy, pain, fatigue, and global health perceptions.Higher scoring indicates poor quality of life. Cronbach alpha in this study ranged from .76 to .89.

Results

Descriptive Statistics and Correlations

The age range of the programme completers was 22-65 years old. The mean age was 47.79 ± 11.67and the Body Mass Indexwas 26.04 ± 5.69 indicating overweight category. The level of depression was mild to moderate (mean=17.10 ± 8.70).Participants wore the device for a mean of 6.26 ± 1.24 days. The mean wear time per days with valid wear time was 13.40 ± 2.61 hours/day. Participants spent 515.33 ± 155.71 min/day in sedentary time, 31.59 ± 25.83 min/day in moderate to vigorous PA (MVPA) and 7.545,02 ± 5.212,95 steps/day. Vigorous physical activity was recorder for only three participants at a very low rate; therefore vigorous activity was merged with moderate intensity physical activity. Descriptive statistics for objectively measured PA are presented below in Table 1.

Table 1. Descriptive statistics of subjectively and objectively measured PA

Variables	*Minimum*	*Maximum*	*M*	*SD*
Valid Days	3	7	6.26	1.24
Wear time hours/valid wear days	9.59	19.10	13.40	2.61
Kcals/day	137.10	1107.10	369.50	222.93
Sedentary time min/day	321.14	870	515.33	155.71
LPA min/day	82.50	502.86	266.01	100.74
MPA min/day	.67	88.71	31.19	24.90
VPA min/day	.00	6	.40	1.39
MVPA min/day	.67	90.29	31.59	25.83
Steps/day	2673.17	24634.43	7545.02	5212.95
Counts/min	70.43	416.74	174.57	96.32

Kcals: kilocalories per day; LPA: light physical activityminutes per day: MPA: moderate physical activity minutesper day; VPA: vigorous physical activityminutes per day; MVPA: moderate to vigorous physical activity minutesper day; Wear time hours/valid wear days: wear time in hours per valid wear days.

Descriptive statistics and Cronbach's alpha coefficients for the psychometric variables are presented in Table 2. In general, participants scored mild to moderate on depression; moderately on the dimension of mood, and in particular below the median point for positive energy and relaxation, and above the median point for tiredness and negative energy; and moderately for the dimension of quality of life.

Correlations between physical activity indices and psychometric variables are presented in Table 2. The results showed moderate negative relationships between moderate to vigorous physical activity and depression, and low negative relationships between walking and depression. In addition the correlations revealed, (a) moderate positive relationships between moderate to vigorous physical activity and dimensions of positive mood, (b) moderate negative relationships between moderate to vigorous physical activity and dimensions of negative mood, (c) moderate positive relationships between walking and dimensions of positive mood, and interestingly (d) moderate positive relationships between walking and dimensions of negative mood. Finally, quality of life demonstrateda low positive correlation with moderate to vigorous physical activity and low negative correlation with walking.

Table 2. Descriptive statistics, Cronbach's alpha and correlations for the psychometric variables and relationships with walking and moderate-vigorous physical activity.

Variables	alpha	M	SD	LPA	MVPA	1	2	3	4	5	6	7
1.Depression		17.10	8.70	-.14	-.48							
2.Positive energy	.92	2.92	1.07	.14	.27	-.73						
3.Relaxation	.65	2.40	0.63	.28	.20	-.53	.58					
4.Tiredness	.94	3.17	1.10	.12	-.20	.87	-.64	-.45				
5.Negative energy	.89	3.16	1.08	.43	-.19	.61	-.54	-.27	.71			
6.SF Physical	.76	16.89	3.28	-.08	.05	-.61	.66	.29	-.68	-.53		
7.SF Mental	.85	19.52	3.32	.07	.07	-.71	.85	.64	-.76	-.55	.80	
8.SF Total	.89	36.42	5.76	-.00	.07	-.70	.80	.51	-.77	-.57	.94	.96

Positive energy, relaxation, tiredness, negative energy (*The Four Dimensional Mood Scale -4DMS)*; Depression *(BDI)*; SF Physical*(Physical Domain of Quality of Life)*; SF Mental(*Mental Domain of Quality of Life)*; SF Total (*Total Score of Quality of Life)*

Finally, regression analysis was calculated toexamine the degree to which light physical activity and moderate to vigorous levels of physical activity time could predict depression. Regression analysis with stepwise method was conducted. The results showed that the model yielded a significant prediction, $F(1, 18) = 5.07$, $p < .05$, with only moderate to vigorous physical activity contributing to the prediction of depression (Beta = -.48, $t = -2.25$, $p < .05$). The model predicted 23% of the variance of depression.

Discussion

This study aimed to explorethe antidepressant predictive propertiesof objective habitual physical activity levels in a sample of adult outpatients diagnosed with major depressive disorder.Based on our findings, accelerometer devices were used almost six day per week (Mean= 6.26 days ±1.24) and mirrored an average of 32 minutes (31 minutes and 59 seconds) of moderate to vigorous daily physical activity. This amount of habitual physical activity,which is equalto approximately 192minutes per week, showed significant predictive effects on depression amelioration. It should be stressed that only a very small amount of time (40 seconds±99 seconds) of the 32 minutes represented vigorous physical activity.

Theaccumulation of approximately 192 minutes of moderate to vigorous physical activity levels are congruent with the World Health Organization (2011)guidelines suggesting that150 minutes of moderate physical activity per week are associated with health gains. Also,the daily accumulation of almost 32 ± 25.83 minutes of moderate to vigorous physical activity per dayseems to be similar to the study of Helgadóttir, Forsell and Ekblom (2015) from Sweden, especially with respect to the exclusively depressed subsample which showed

37.75±22.22 minutes of moderate to vigorous physical activity levels.This is an encouraging finding that supports consistency concerning physical activity levels in depressed patients regardless cultural or climate differences. Also, when interpreting our study findings in combination with the findings fromHelgadóttir, Forsell and Ekblom (2015), it is seen that physical activity is inversely related with depression and visa versa. Also, our findings seem to concur with the recent meta-analytic findings (Schuch, Vancampfort, Firth et al., 2017) wheredepressed outpatients exhibited 29.79 minutes of moderate to vigorous physical activity.

With respect to sedentary time, our study revealed that depressed patients displayed an average of 8 hours and 35 minutes of sedentary time per day (during waking hours). In line to our findings, a recent meta-analysis that examinedstudies with objective or self-report levels of physical (in)-activity in patients with major depressive disorder has reported 8.5 hours of average sedentary time(Schuch, Vancampfort, Firth et al., 2017).Collectively, our findings regarding levels of moderate to vigorous physical activity as well as levels of sedentary time are highly consistent with previous studies. Also, our findings seem to be dissociated with the fact that specific physical activity components such as work- or house-related activities are not connected with lower mental health problems (White, Babic, Parker et al., 2017).

In addition, our study revealed an encouraging association between moderate to vigorous physical activity with mood. In particular, moderate to vigorous physical activity showed positive associations with mood indices referred to positive energy and relaxation and negative association with mood indices referred to tiredness and negative energy. However, correlation coefficients did not reach a level of statistical significance presumably due to small number of participants. This positive trend between moderate to vigorous physical activity and mood could be integrated with the frame of depressive disorder as low mood represents a core component of depression. Apart from our study where moderate to vigorous physical activity showed a high and significant correlation with depression ($r= -.48$, <0.05), Wielopolski, Reich, Clepce et al. (2015) have also found a high and significant correlation between physical activity and depression in adult inpatients with major depressive disorder. The same association has been recorded in college students (Hu, 2008).

Finally, quality of life measures were unrelated to light or moderate to vigorous physical activity levels. Although exercise is associated with better quality of life(Callaghan, Khalil, Morres et al., 2011), physical activitydid not seem to be associated with such benefits in this study on account of potential overlapping connection with depression.

Despite the promising findings of this study indicating the prediction of depression relief by moderate to vigorous physical activity levels, there are some important limitations

that need to be considered. First, the small number of participants raises serious doubtsabout the generalizability of findings. In addition, participants might have mirrored higher than usual moderate to vigorous physical activity levels as a result of increased motivation to participating in the study. Also, the lack of measures related to outcome expectations or social desirability represents another significant limitation in this study. To this extent, the study findings should be interpreted with caution.

Nevertheless, the study has a number of key strengths that need to be considered. These included the objective measure of habitual physical activity and the recruitment of adult (18-65) outpatients with a clinical diagnosis of major depressive disorder.

In conclusion, although generalizability cannot beconfirmed due to a small number of patients, the homogenous and clinically defined sample, the objective measurement of habitual physical activity levels, the prediction of depression relief by moderate to vigorous physical activity and the consistency of themain finding with previous studies highlight the importance of (i) the study findings and (ii) replicating the current study with a larger sample and a longitutinal design to record bio-directionality between physical activity and depression.

Chapter 7. General Discussion and conclusions

The current Thesis aimed at contributing to (i) the clarification of the causal association between exercise participation and improved clinical depression, (ii) the elicitation of evidence-based grounds from SDT in order to improve depression andincrease physical activity participation rates and (iii) the explanation of objective meaures of habitual physical activity in relationship to depression. Accordingly, this Thesis presented evidence favouring(i) the causal association between aerobic exercise and depression amelioration (ii) the employment of SDT in order to improve severity of depression andrates of physical activity participation and (iii) the promotion of a physically active lifestyle to decrease depression severity.

Study-1 was a critical review,which provided a comprehensive and descriptive view on the literature trends regarding exercise and major depressed adult patients. Findings suggested that exercise for adult patients with major depressive disorder was an effective antidepressant intervention. Also, sceptical interpretations were emerged regarding the effectiveness of the rationale of current practice with respect tophysical activity and exercise on prescription schemes for patients with depression. Based on previous research findings emerged from SDT, the study provided a series of theoretically-based suggestions as to how more effective exercise on prescription protocols could beoperated for the treatment of depressed patients.

Study-2 was a systematic review that investigated the optimum dose-response relationship between exercise and depression relief in clinically diagnosed adult patients (18-65years old) with major depressive disorder. Findings indicated clinically significant antidepressant effects for exercise in half of reviewed trials. Specifically, both short- and longer-term exercise of three times per week for 3, 8, 9 weeks led to an improvement in depression that was equivalent to a normal population range. Risk of bias evaluation, however, revealed a moderate design quality for reviewed trials. Although the optimum dose-response relationship between exercise and depression could not be defined due to limited evidence rather lack of evidence, it should be highlighted that the most effective dose-response relationship identified in this study is consistent to physical activity guidelines for the treatment of depression and to meta-analytic reviews with separate evaluation on clinical samples. Thus, our findings seemed to support the causal interpretation of the association of exercise participation with depression relief.

Study-3was a systematic review and meta-analysis that reviewed the antidepressant effects of aerobic exercise in comparison to routine practice treatment conditions in adult

patients (18-65years old) diagnosed with major depressive disorder. Based on twelve eligible RCTs reviewed, aerobic exercise showed a significantly large overall treatment effect on depression displaying low heterogeneity levels. Further, no publication bias was recorded. Data pooled from 24 sensitivity analyses regarding patient/intervention characteristics pointed statistically significant large or moderate to large treatment effects for aerobic exercise conducted (i) three times per week with both short- or longer-term duration (up to 4 weeks, or 8-12 weeks), (ii)in both outdoor and indoor settings, (iii) with lower (>15%) or higher (>15%) dropout rates, and iii) across inpatients and outpatients with various levels of age range or depressive symptom severity. Similar results for exercise were found when coding of active comparators separated treatments for depression into biological- (antidepressant drugs) or psychological-based (psychotherapy). Across the 24 sensitivity analyses, heterogeneity was low or moderate (≤40%) and non-statistically significant apart from two data set with younger age range and individual exercising, where heterogeneity was 52.78% and 53.59% and marginally statistically significant and non-significant, respectively. Finally, coding for risk of bias did not influence the results, indicating the association of the antidepressant effects of exercise with lower risk of bias. Notwithstanding the limited number of RCTs reviewed, findings are in line to physical activity guidelines for the treatment of depression supporting the causal antidepressant effect of aerobic exercise.

Study-4 was an cross sectional study that explored potential SDT-based pathways towards depression relief andphysical activity participation in a sample of 206 adult outpatients (18-65 years old) with major depressive disorder who were predominantly (67%) sedentary. Particularly, satisfaction of the psychological needs for competence, autonomy and relatedness was associated withsignificant predictive effects on depression relief and onphysical activity participation including the corresponding metabolic equivalents.Importantly, need satisfaction overcame the mediating impact of autonomous behavioural regulation in the above predictions. Also,controlling forms of behavioural regulation where physical activity participation deals with external gains or self-criticism detected a non-significant but adverse effect on depression as well as onphysical activity participation. Finally, depression revealed a toxic effect on the need satisfaction indicating the necessity to provide advanced fostering of need satisfaction. To this extent, it is important to note that controlling forms of behavioural regulation (e.g., exercise for health gains) that comprise the traditional physical activity on prescription or promotion consultancy frameshowed to be carrying ineffectiveproperties in increasing physical activity participation or ameliorating depression. Conversely, advanced facilitation of need satisfaction referring to

competence, autonomy and relatedness emerged as the key factor towards depression relief and physical activity participation.

Study-5 was a cross sectional study that aimed at investigating the association of objective measuresof habitual physical activity levels with depression in 19 outpatients with major depressive disorder aged 18-65 years who were referred to the study by mental health professionals responsible for their treatment.In detail, objectively measured physical activity at moderate to vigorous intensity showed an inverse association with depression as it showed statistically significant predictive power towards depression relief. It should be underlined, however, that the amount of vigorous physical activity was inconsiderable as it amounted to 40 seconds ± 99 secondson average.The findings of the study receive further merit given that the physical activity levels of the study participants corresponded to the guidelines of the World Health Organisation.Particularly,whereasthe World Health Organisation recommends 150min of moderate physical activity per week, the study participants mirrored an average accumulation of 180min of moderate to vigorous intensity per week. It was equally encouraging that the predictive power of the moderate to vigorous intensity explained 23% of depression variance. Notwithstanding the small sample size and the potentially positive impact of theaccelerometers use on the adoption of higher than usual physical activity levels for the shake of the study, a depression ameliorating physically active lifestyle among major depressed adult outpatients seems to be a feasible scenario.

Future research

With respect to study 4, this Thesis suggests that further research is needed to specify the most influential autonomous-, relatedness- and competence-supportive agents and components for exercise in sedentary adult outpatients with major depressive disorder. Also, replication of the fourth study of this Thesis with the adoption of a longitudinal design is highly recommended in order to enable researchers draw causal inferences regarding the reciprocal relationship between depression and physical activity with the SDT premises. In addition, it is essential the fifth study of this Thesis to be replicated in a larger group of patients while controlling for potential confounders such as social desirability or outcome expectations.

A convincing corpus of clinical RCTs and meta-analytic reviews has repeatedly presented evidence for the antidepressant effects of exercise. However, more clinical RCTs in major depressed adult patients are needed to provide internally valid evidence regarding the following currently unexplored issues: (i) the long-term antidepressant effects of exercise, (ii)

the potential side effects associated with exercise participation, and (iii) the potential influence of outcome expectations on treatment outcomes.

Clinical RCTs represent the gold standard of evidence that measure efficacy, defined as “the benefit a treatment produces under ideal conditions, often using carefully selected subjects in a research clinic” (Roland and Torgerson, 1998). Nevertheless, clinical RCTs suffer external validity; they are restricted to recruiting via diagnosis and narrow inclusion criteria, to specific settings and to one or two primary outcomes unable to scan the syndrome of depression. The lack of external validity properties, however, inhibits translation of clinically evident efficacy by routine practice.

Pragmatic RCTs instead, arebased on externally valid criteria and measure effectiveness defined as “the benefit the treatment produces in routine practice” (Roland and Torgerson, 1998). Thus, pragmatic trials provide routine practice with translational evidence attributable to increased external validity.

Hence, further research is needed to translate clinical evidence into routine practice know-how in order to enable decision-making bodies and clinicians proceed accordingly. For this purpose, Schuch, Morres, Ekkekakis et al. (2016), Schuch, Morres, Ekkekakis et al. (2017) andEkkekakis and Murri (in press) have recently highlighted the importance of carrying out exercise RCTs with a pragmatic design for people with depression. Thanks to increased external validity, the pragmatic design is capable of replicating routine practice conditions on account of a series of methodological criteria. These refer to i) implementation of the intervention in commonly available facilities ii) inclusion of patients presenting symptoms or problems related to depression as opposed to specific diagnosis, iii) employment of minimum exclusion criteria in order to recruit heterogeneous samples and enable participation of patients with a wide range of clinical features (both somatic and psychological) that often challenge routine practice treatment effectiveness, iv) design suitability to compare usual to new treatments while varying the intervention to the patient’s key problem v) primary outcome measures to record depression relief and vi) functional outcome measures to document the overall quality of life and psychosocial functioning improvement (Ford and Norrie, 2016; Hotopf, 2002; MacPherson, 2004; March, Silva, Compton et al., 2005; Tunis, Stryer and Clancy, 2003).

Moreover, the pragmatic design, in contrast to clinical design, is capable of integrating a fundamental methodological characteristic of exercise intervention that is often seen as a significant methodological flaw. Specifically, due to nature of the exercise intervention, clinical RCTs comparing exercise to other antidepressant treatments cannot blind patients and

therapists. Although this methodological flaw is also found in classical antidepressant treatments such as psychotherapy (Seligman, 1995), lack of double-blinding could be seen as a cause of inconclusive interpretations on the robustness of the anti-depressiveness of exercise in clinical settings. The pragmatic design, however, does not consider lack of double-blinding a methodological flaw because routine clinical practice is also not blinded (March et al., 2005). Indeed, trials with blinded interventions cannot be considered fully pragmatic (Ford and Norrie, 2016). Thus, field experts stress that the pragmatic design is an ideal platform that provides evidence of effectiveness by replicating routine practice conditions without considering lack of double-blinding a methodological flaw (Ford and Norrie, 2016; Hotopf, 2002; March, Silva, Compton et al., 2005).

Another major advantage of the pragmatic design deals with its suitability to compare usual to new treatments while varying the intervention to the patient's key problem (MacPherson, 2004; Tunis, Stryer and Clancy, 2003). Varyingthe intervention to the patient's key problem is of major importance given that prescribed intensity exercise relies on fixed range of intensity and might not be able to treat the multifaceted and often antithetic status of the syndrome of depression among patients; for example, depression can be characterized either by psychomotor agitation or by psychomotor retardation(American Psychiatric Association, 2013). Moreover, varying the intensity may enable patients to exercise at low or very low intensity exercise. This is likely in light of the identical characteristics of major depression with the overtraining syndrome where overt-rained athletes are prescribed antidepressant medication and exercise at low intensities (Armstrong and VanHeest, 2002).

Considering the advantages of pragmatic design, Callaghan, Khalil, Morres et al. (2011)has conducted the only currently available pragmatic RCT for depressed women and found a favourable comparison of self-determined (preferred) intensity exercise to prescribed intensity exercise. In particular, the trial recorded higher antidepressant, self-esteem and quality of life effects although the intervention was conducted for only four weeks (3 times/per week), in commonly available exercise settings and in a community-based depressed sample comprising mainly long-term mental health services users. Further, the superiority of of the self-determined intensity exercise in comparison to prescribed intensity exercise is emphasized by the fact that both groups experienced an improvement in social support delivered by exercise programme supervisors. Although this finding cannot rule out the importance of social support, it seems that social support may not play a key-role role in exercising depressed patients (Morres, Van de Vliet, Knapen et al., 2003), whereasself-determined intensity exercise could stand by itws own right.Further, self-determined intensity

exercise on the basis of personal preferences has been suggested as an important strategy in clinical settings (Morres, 2003). Further, preliminary evidence from secondary analysis of the data byCallaghan, Khalil, Morres et al. (2011) on the basis of intra-individual analysis of whether treatment effectiveness mirrored reliable changes in depression beyond the standard error of measurement and within the normal population range indicated that (i) no participant experienced reliable deterioration in depression, and (ii) almost a third of the patients (32%) showed recovery coefficients given that the improvement in depression was ranked beyond the standard error of measurement and within the normal population range (Morres, Callaghan, Hinton-Bayre et al., 2014; Morres, Callaghan, Hinton-Bayre et al., in submission).

Despite the optimistic findings of this trial derived from intention-to-treat data analysis(Callaghan, Khalil, Morres et al., 2011), a number of unfulfilled criteria stress the replication of this pragmatic trial before drawing firmer conclusions on whether the anti-depressiveness of self-determined exercise intensity can be seen as comprehensively explored. These criteria refer primarily to (i) the relative small number of participants (38 participants), (ii) the lack of process evaluation in terms of the implementation of intervention and (iii) the short-term intervention period (4 weeks) compared to the period of 10-14 weeks that guidelines recommend for the treatment of depression through physical activity (Nattional Institute for Health and Care Excellence (NICE), 2009). By fulfilling the above criteria the robustness of the rationale referring to the antidepressant effectiveness of self-determined intensity exercise is expected to be scaled-up.

Implications for practice

Physical activity and exercise on prescription for people with various disorders including depression has been (or is being) developed in various European countries, especially after the release of relevant guidelines by the European Commission (2008). Clinical evidence derived from the second and third study of this Thesis supported the causal effect of physical exercise on depression. Thus, exercise on prescription for patients with clinical depression is seen a valuable strategy. The recently established “European Initiative for Exercise in Medicine” (http://exerciseismedicine.eu) aims at making “physical activity and exercise a standard part of a European disease prevention and treatment medical paradigm”. This initiative, however, needs to be cautiously developed since the widely used iatrogenic modelling of the promotion or prescription of physical activity/exercise (exercise for health benefits) has illustrated high dropout rates among depressed patients, which werehigher compared to other patients. Nevertheless, current guidelines of this initiative lie

upon the iatrogenic modelling; exercise is promoted or prescribed on iatrogenic basis where motivation is considered a uni-dimensional construct consisted of external motives referring to the need to gain health benefits as a result of relevant recommendations by the health professional responsible for treatment.

However, dropping out from physical activityon prescription is a complex phenomenonthat it is not exclusively consisted of insufficient health-oriented motivation; dropping out from exercise referral schemes involves biopsychosocial determinants and it is mainly related with psychosocial factors (Johnston, Warwick, De Ste Croix et al., 2005). Moreover, some of these factors may represent actual and not perceived barriers. For example, lack of time is a universal exercise barrier, and, potentially, an actual barrier for depressed patients; mental health episodes cause time pressure and adversely affect exercise adherence (Stetson, Rahn, Dubbert et al., 1997) while exercise is perceived as more time-demanding than other health behaviors (Turk, Rudy and Salovey, 1984). Thus, lack of time could be, indeed, an actual dropout factor especially since depressed patients report i) problems in dealing with daily life activities (Simmons and Kritchevsky, 1993) and ii) time mismanagement as the top exercise barrier (O'Neal, Dunn and Martinsen, 2000). In support of this scenario, Stathi, Milton and Riddoch (2006) recorded claims that exercise on prescription timetables are often inflexible or inconvenient.

Also, a potentially actual barrier seems to be the "treatment room" itself; gym facilities (treatment room) where exercise on prescription is usually operated seem to be incompatible to the patients' needs. After conducting exercise programmes for depressed patients in a sport centre (Biddle, Backhouse and Faulkner, 2004), Biddle (2005) stated that gyms may not fit for all. Indeed, exercise barriers are seen an intimidating gym atmosphere and a dislike of the music and TV operation (Morgan, Battersby, Weightman et al., 2016) or the noise of the weight lifters in a male dominated gym (Stathi, Milton and Riddoch, 2006). A few months ago (December 2016), the Trinity Sports and Leisure in Bridgwater, Somerset, which operates on behalf of Sedgemoor District Council in the UK, announced "quite and music-free sessions" operation at lunchtime for gym users striving to rest their brain from the widespread audio-visual stimulation of our times. Also, it has been reported that general announcements over loudspeakers and other audio systems will be stopped during this time (http://www.healthclubmanagement.co.uk/health-club-management-news/Fitness-quite-gym/328737).

Another actual barrier towards exercise participation might involve the professionals themselves. The majority of the exercise on referral schemes were originally established to

provide physical health benefits, thus, staff are typically exercise scientists non-specialised in mental health disorders, who may not be capable of effectively supervising mental health patients (Crone, Johnston, Gidlow et al., 2008). Tis is an important aspect of service delively especially since the patients themselves have also stressed the importance of being supervised by exercise scientists who are familiar with mental health (Mental Health Foundation, 2009).

Given this complexity, physical activity/exercise on prescription may not mirror lower dropout rates as long as long as participation is (i) considered a "narrow framing" phenomenon lacking externally regulated motivation, (ii) supported with health-oriented consultancy, and (iii) treated within a context where specialised staff, fundamental infrastructural changes and a series of psychosocial interventions (e.g., relapse prevention strategies, behavioural modification, etc) appear to be indisputably essential.

Due to the great deal of reforms or reconsiderations, an alternative scenario is currently essential to tackle the high dropout rates of depressed patients from physical activity/exercise on prescription schemes. This Thesis followed the scenario of searching strong theoretical grounds totrace a predictive motivational gridto depression relief and to physical activity participation. The selection of this scenariowas based on SDT and involved consideration that mental health patients reveal strong preferences for the exercise treatment (Fleischmann, 2003; Sigurdsson, Ólafsdóttir and Gottfredsson, 2008; Ussher, Stanbury, Cheeseman et al., 2007), show high motivation upon prescription endorsement (Crone, Johnston, Gidlow et al., 2008; Harrison, McNair and Dugdill, 2005), and mirror SDT dendrites as strong predictors or correlators of physical activity participation (Sørensen, 2006; Vancampfort, Moens, Madou et al., 2016).

Therefore, this Thesis investigated pathways of motivation towards physical activity participation by employing an SDT-based exercise modeling. SDT considers motivation a multi-dimensional structure and shows fruitful potentials in mental health patients attributable to previous work by Sørensen (2006) and Vancampfort, Moens, Madou et al. (2016). In SDT, behavioural regulation is consisted of both extrinsically driven and intrinsically generated regulators (or types of motivations) whereas the satisfaction of the three basic psychological needs of competence, autonomy and relatedness is catalysing the internalization of behavioural regulation. Specifically, behavioural regulation is seen as the mediating factor between psychological needs and behavioural performance that interplays in proportion to the degree of need satisfaction. Hence, SDT is capable of simultaneously testing the construct of (i) the widely used iatrogenic modelling of exercise that is promoting physical activity through controlling forms of behavioural regulation (extrinsic motivation), and (ii) the

proposed exercise modelling that promotes physical activity through autonomous forms of behavioural regulation (intrinsic types of motivation). Further, SDT indicates that need satisfaction is triggering performance behaviour, however, this is realised through the mediating effect of behavioural regulators, which act as mediating factors.

Outcomes of this Thesis revealed that psychological needs emerged as the most important SDT factor attributable to their leading and direct role in predicting depression relief or physical activity participation. However, depression appeared, in addition, to be carrying adverse effects on need satisfaction. Both findings are reasonable given that the sample of this study (study-4) was predominantly sedentary. To this extent, behavioural regulators were presumably premature, non-existing, or unimportant for the study sample. Hence, in this Thesis, behavioural regulators did notplay the mediating role that SDT postulates. Therefore, notwithstanding the inability to provide any prospective or causal outline due to the non-longitudinal design of the study, it is acknowledged that facilitation of need satisfaction seems to be a preceding factor to physical activity participation. However, need satisfaction is infected by depression. As such, a substantial fostering of need satisfaction by clinicians appears to be the cornerstone of consultancy towards physical activity participation. Relevant recommendations regarding fostering of psychological needs have been presented by Morres, Stathi, Martinsen et al. (2014).Finally, it should be acknowledged that controlling forms of behavioural regulation representing the most widely used consultancy form in physical activity on prescription or promotion schemes demonstrated no predictive effect on depression or on physical activity participation in this Thesis. This is an important finding that needs to be taken into consideration; routine practice for physical activity/exercise on prescription or on promotion is typically based on controlling forms of behavioural regulation as motivation inputs deal with external gains, specifically, health benefits.

Finally, this Thesis has found that habitual physical activity appears to be associated with depression amelioration (study 5). Specifically, moderate to vigorous physical activity levels exhibited predictive effects on depression relief. Based on these findings, clinicians need to take into consideration that promoting habitual physical activity at moderate to vigorous levels may enable adult depressed outpatients with major depressive disorder to experience an improvement in depression. Although no causal inferences can be drawn attributable to the non-longitutinal design of study 5, literature suggests that physical activity is associated with depression relief. Thus, satisfying psychological needs for competence, autonomy and relatedness in exercise (found in the fourth study), may lead to the benefits that

habitual physical activity has shown in the fifth study of this Thesis. It should also be stressed that themoderate to vigorous level of physical activity recorded in this Thesis is widely associated with physical health-enhancing benefitsas well. Giventhat depressed patients are twice as likely to die prematurely compared with the general population due to various causes including sedentary-related disorders such as cardiovascular disease (Ösby, Brandt, Correia et al., 2001),moderate to vigorous habitual physical activity could act as an invaluable “polypill” intervention ensuring both physical and mental health benefits.

Limitations

The reviews of this Thesis (study1, 2, and 3) included a limited number of reviewed trials. To this extent, more trials with adult depressed patients are needed to increase further our understanding on the causal antidepressant impacts of physical exercise that was seen in this Thesis. With respect to study 4, further research is needed to specify the most influential autonomous-, relatedness- and competence-supportive agents and components for physical activity participation in sedentary adult outpatients with major depressive disorder. Finally, the cross sectional design of the studies 4 and 5 of this Thesis does allow causal interpretations of the findings. To this extent, replication of the above studies with a longitutinal design is essential in order to draw causal conclusions.

APPENDICES

Σημάδεψε με έναν σταυρό την πρόταση που διάλεξες.
Ημερομ.

Διαλέξτε από κάθε ομάδα εκείνη τη μια πρόταση η οποία περιγράφει με τον πιο καλό τρόπο το πώς νιώθατε την ΕΒΔΟΜΑΔΑ ΠΟΥ ΠΕΡΑΣΕ, ΣΥΜΠΕΡΙΛΑΜΒΑΝΟΝΤΑΣ ΚΑΙ ΤΗΣ ΣΗΜΕΡΙΝΗΣ ΗΜΕΡΑΣ.

Αν νομίζετε ότι ισχύουν περισσότερες από μια προτάσεις της ίδιας ομάδας, σημαδέψτε αυτές που νομίζετε ότι ισχύουν. Προτού διαλέξτε, διαβάστε όλες τις προτάσεις της κάθε ομάδας.

1	□ Δεν νιώθω **θλιμμένος.** □ Νιώθω θλιμμένος. □ Νιώθω συνέχεια θλιμμένος και δεν μπορώ να το αποδιώξω αυτό. □ Είμαι τόσο θλιμμένος ή δυστυχισμένος, που δεν μπορώ να το αντέξω.
2	□ Δεν νιώθω καμία ιδιαίτερη **αποθάρρυνση** όσο αφορά στο μέλλον. □ Νιώθω να μην έχω κουράγιο για το μέλλον □ Νιώθω πως δεν έχω να περιμένω τίποτα από το μέλλον. □ Νιώθω πως δεν υπάρχει καμία ελπίδα για το μέλλον και πως τα πράγματα δεν πρόκειται να καλυτερέψουν.
3	□ Δεν νιώθω **αποτυχημένος.** □ Νιώθω πως είμαι περισσότερο αποτυχημένος από το μέσο όρο. □ Όταν σκέπτομαι τη ζωή μου, το μόνο που βλέπω είναι μια σειρά από αποτυχίες. □ Νιώθω ό,τι είμαι εντελώς αποτυχημένος σαν άτομο.
4	□ Παίρνω από τα πράγματα την ίδια **ικανοποίηση** που έπαιρνα πάντοτε. □ Δεν χαίρομαι με τα πράγματα έτσι όπως τα χαιρόμουνα. □ Τίποτα δεν μου δίνει πραγματική ικανοποίηση. □ Είμαι ανικανοποίητος με τα πάντα ή βαριέμαι τα πάντα.
5	□ Δεν νιώθω καμία ιδιαίτερη **ενοχή** □ Νιώθω ένοχος κάμποσες φορές. □ Νιώθω σχετικά ένοχος τον περισσότερο καιρό. □ Νιώθω ένοχος συνέχεια
6	□ Δεν έχω την αίσθηση ότι **τιμωρούμαι** για κάτι. □ Έχω την αίσθηση ότι ίσως να τιμωρούμαι. □ Περιμένω πως θα τιμωρηθώ. □ Νιώθω ότι τιμωρούμε.

7	□ Δεν αισθάνομαι **απογοήτευση** με τον εαυτό μου. □ Είμαι απογοητευμένος με τον εαυτό μου. □ Ο εαυτός μου με αηδιάζει. □ Μισώ τον εαυτό μου.
8	□ Δεν νιώθω περισσότερο άσχημα απ' ό,τι ο οποιοσδήποτε άλλος. □ Κριτικάρω τον εαυτό μου για τις **αδυναμίες** ή τα λάθη μου. □ Συνεχώς κατηγορώ τον εαυτό μου για όσα στραβά έχω. □ Κατηγορώ τον εαυτό μου για καθετί κακό που συμβαίνει.
9	□ Δεν μου περνά καμία σκέψη να **σκοτωθώ.** □ Μου έρχονται σκέψεις να σκοτωθώ, αλλά δεν τις πραγματοποιώ. □ Θα ήθελα να σκοτωθώ. □ Θα σκοτωνόμουνα αν μου δίνονταν η ευκαιρία.
10	□ Δεν **κλαίω** περισσότερο από το συνηθισμένο. □ Τώρα κλαίω περισσότερο απ' ό,τι παλιότερα. □ Τώρα κλαίω συνέχεια. □ Κάποτε μπορούσα κι έκλαιγα, όμως τώρα δεν μπορώ να κλάψω παρ' όλο που το θέλω.
11	□ Δεν είμαι τώρα περισσότερο **εκνευρισμένος** απ' ό,τι είμαι συνήθως. □ Ενοχλούμε ή εκνευρίζομαι πιο εύκολα απ' ό,τι είμαι συνήθως. □ Τώρα συνεχώς νιώθω εκνευρισμένος. □ Δεν με εκνευρίζουν διόλου τα πράγματα που κάποτε μ' εκνεύριζαν.
12	□ Δεν έχω χάσει το **ενδιαφέρον** μου για τους άλλους ανθρώπους. □ Ενδιαφέρομαι για τους άλλους λιγότερο απ' ό,τι ενδιαφερόμουν πριν. □ Έχω χάσει το περισσότερο ενδιαφέρον μου για τους άλλους. □ Έχω χάσει κάθε ενδιαφέρον για τους άλλους.
13	□ Παίρνω **αποφάσεις** περίπου το ίδιο καλά όσο πάντοτε. □ Αναβάλλω τις αποφάσεις μου πιο συχνά απ' ό,τι τις ανέβαλλα πριν. □ Δυσκολεύομαι περισσότερο στο να πάρω αποφάσεις σε σύγκριση με παλιότερα. □ Δεν παίρνω πια καμία απόφαση.
14	□ Δεν έχω την αίσθηση ό,τι έχω χειρότερη **εμφάνιση** απ' ό,τι παλιότερα. □ Μ' ανησυχεί το ό,τι δείχνω γερασμένος ή όχι ελκυστικός. □ Έχω την αίσθηση ό,τι η εμφάνιση μου άλλαξε οριστικά, έτσι που να μη δείχνω ελκυστικός. □ Πιστεύω πως δείχνω άσχημος.
15	□ **Εργάζομαι** το ίδιο καλά όσο πάντοτε. □ Χρειάζεται να καταβάλλω επιπλέον προσπάθεια για να ξεκινήσω να κάνω κάτι.

	□ Αναγκάζομαι να πιέσω παρά πολύ τον εαυτό μου για να κάνω οτιδήποτε. □ Δεν μπορώ να κάνω καμία απολύτως δουλειά.
16	□ Μπορώ να **κοιμάμαι** το ίδιο καλά όπως συνήθως. □ Δεν κοιμάμαι τόσο καλά όσο κοιμόμουνα. □ Ξυπνώ 2-3 ώρες νωρίτερα από το συνηθισμένο και δυσκολεύομαι να ξανακοιμηθώ. □ Ξυπνώ πολλές ώρες νωρίτερα από το συνηθισμένο μου και μετά δεν μπορώ να ξανακοιμηθώ.
17	□ Δεν **κουράζομαι** περισσότερο απ' το συνηθισμένο. □ Κουράζομαι ευκολότερα απ' ό,τι κουραζόμουν πριν. □ Κουράζομαι με σχεδόν ό,τι και αν κάνω. □ Είμαι τόσο κουρασμένος που δεν κάνω τίποτα.
18	□ Η **όρεξη** μου δεν είναι χειρότερη απ' ό,τι συνήθως. □ Η όρεξη μου δεν είναι τόσο καλή όσο ήταν πριν. □ Η όρεξη μου τώρα έχει χειροτερέψει. □ Δεν έχω πια καθόλου όρεξη.
19	□ Δεν έχω χάσει καθόλου (ή πολύ) **βάρος** τελευταία. □ Έχω χάσει περισσότερο από 3 κιλά. □ Έχω χάσει περισσότερο από 5 κιλά. □ Έχω χάσει περισσότερο από 8 κιλά. Επίτηδες προσπαθώ να χάσω βάρος τρώγοντας λιγότερο: ___ναι ___όχι
20	□ Η **υγεία** μου δεν μ' ανησυχεί περισσότερο από το συνηθισμένο. □ Ανησυχώ για σωματικά προβλήματα μου όπως πόνοι ή ανακατωμένο στομάχι ή δυσκοιλιότητα. □ Μ' ανησυχούν πολύ τα σωματικά προβλήματα και δύσκολα σκέφτομαι κάτι άλλο έξω απ' αυτά. □ Μ' ανησυχούν τα σωματικά μου προβλήματα τόσο πολύ που δεν μπορώ να σκεφτώ τίποτα άλλο.
21	□ Δεν έχω παρατηρήσει πρόσφατα καμία αλλαγή στο ενδιαφέρον μου για **σεξ.** □ Ενδιαφέρομαι για σεξ λιγότερο απ' όσο ενδιαφερόμουν πριν. □ Τώρα ενδιαφέρομαι πολύ λιγότερο για το σεξ. □ Έχω χάσει κάθε ενδιαφέρον για το σεξ.

Οι παρακάτω ερωτήσεις αφορούν τους λόγους για τους οποίους θα συνέχιζες να γυμνάζεσαι. Σημειώστε κατά πόσο οι δηλώσεις ισχύουν για σένα κυκλώνοντας έναν αριθμό για κάθε δήλωση.

Παράδειγμα:	**Σίγουρα Όχι**	**Όχι**	**Δεν είμαι σίγουρος/η**	**Ναι**	**Σίγουρα ναι**
Θα συνέχιζα να γυμνάζομαι για να βελτιώσω την υγεία μου.	0	1	2	3	4

	Θα συνέχιζα να γυμνάζομαι επειδή ...	**Σίγουρα όχι**	**Οχι**	**Δεν είμαι σίγουρη/ος**	**Ναι**	**Σίγουρα Ναι**
1	Θα συνέχιζα να γυμνάζομαι επειδή λένε πως πρέπει.	**0**	**1**	**2**	**3**	**4**
2	Θα συνέχιζα να γυμνάζομαι επειδή αισθάνομαι ενοχές όταν δεν γυμνάζομαι.	**0**	**1**	**2**	**3**	**4**
3	Θα συνέχιζα να γυμνάζομαι επειδή εκτιμώ τα οφέλη της γυμναστικής.	**0**	**1**	**2**	**3**	**4**
4	Θα συνέχιζα να γυμνάζομαι επειδή είναι διασκεδαστικό.	**0**	**1**	**2**	**3**	**4**
5	Δεν βλέπω γιατί πρέπει να γυμνάζομαι.	**0**	**1**	**2**	**3**	**4**
6	Θα συνέχιζα να γυμνάζομαι επειδή οι άλλοι (φίλοι, οικογένεια, σύντροφος, γιατρός) λένε πως πρέπει.	**0**	**1**	**2**	**3**	**4**
7	Θα συνέχιζα να γυμνάζομαι επειδή αισθάνομαι άσχημα όταν χάνω ένα πρόγραμμα γυμναστικής.	**0**	**1**	**2**	**3**	**4**
8	Θα συνέχιζα να γυμνάζομαι επειδή είναι σημαντικό για μένα να γυμνάζομαι συστηματικά.	**0**	**1**	**2**	**3**	**4**
9	Δεν βλέπω τον λόγο γιατί θα πρέπει να μπαίνω στον κόπο να γυμνάζομαι.	**0**	**1**	**2**	**3**	**4**
10	Θα συνέχιζα να γυμνάζομαι επειδή ευχαριστιέμαι τα προγράμματα γυμναστικής στα οποία συμμετέχω	**0**	**1**	**2**	**3**	**4**

Οι παρακάτω ερωτήσεις αφορούν τους λόγους για τους οποίους θα συνέχιζες να γυμνάζεσαι. Σημειώστε κατά πόσο οι δηλώσεις ισχύουν για σένα κυκλώνοντας έναν αριθμό για κάθε δήλωση.

Παράδειγμα:	**Σίγουρα Όχι**	**Όχι**	**Δεν είμαι σίγουρος/η**	**Ναι**	**Σίγουρα ναι**
Θα συνέχιζα να γυμνάζομαι για να βελτιώσω την υγεία μου.	0	1	2	[3]	4

Θα συνέχιζα να γυμνάζομαι επειδή ...		**Σίγουρα όχι**	**Οχι**	**Δεν είμαι σίγουρη/ος**	**Ναι**	**Σίγουρα Ναι**
11	Θα συνέχιζα να γυμνάζομαι επειδή οι άλλοι δεν θα ήταν ευχαριστημένοι μαζί μου εάν δεν το έκανα.	**0**	**1**	**2**	**3**	**4**
12	Δεν βρίσκω νόημα στο να γυμνάζομαι.	**0**	**1**	**2**	**3**	**4**
13	Θα συνέχιζα να γυμνάζομαι επειδή αισθάνομαι σαν αποτυχία όταν δεν έχω γυμναστεί για κάποιο διάστημα.	**0**	**1**	**2**	**3**	**4**
14	Θα συνέχιζα να γυμνάζομαι επειδή είναι σημαντικό για μένα να κάνω την προσπάθεια να γυμνάζομαι.	**0**	**1**	**2**	**3**	**4**
15	Θα συνέχιζα να γυμνάζομαι επειδή θεωρώ ότι η γυμναστική είναι μία ευχάριστη δραστηριότητα.	**0**	**1**	**2**	**3**	**4**
16	Θα συνέχιζα να γυμνάζομαι επειδή αισθάνομαι πίεση από τους άλλους (φίλοι, οικογένεια, σύντροφος, γιατρός) να γυμνάζομαι.	**0**	**1**	**2**	**3**	**4**
17	Θα συνέχιζα να γυμνάζομαι επειδή όταν δεν γυμνάζομαι είμαι γεμάτη-ος ενέργεια που θέλω κάπου να την εκτονώσω.	**0**	**1**	**2**	**3**	**4**
18	Θα συνέχιζα να γυμνάζομαι επειδή αντλώ ευχαρίστηση και ικανοποίηση από την γυμναστική.	**0**	**1**	**2**	**3**	**4**
19	Νομίζω πως η γυμναστική είναι χάσιμο χρόνου.	**0**	**1**	**2**	**3**	**4**

Οι παρακάτω ερωτήσεις αφορούν τους λόγους για τους οποίους θα ξεκινούσες να γυμνάζεσαι.
Σημειώστε κατά πόσο οι δηλώσεις ισχύουν για σένα κυκλώνοντας έναν αριθμό για κάθε δήλωση.

Παράδειγμα:	**Σίγουρα Όχι**	**Όχι**	**Δεν είμαι σίγουρος/η**	**Σίγουρα ναι**	**Ναι**
Θα ξεκινούσα να γυμνάζομαι για να βελτιώσω την υγεία μου.	0	1	2	[3]	4

Θα ξεκινούσα να γυμνάζομαι επειδή ...		**Σίγουρα όχι**	**Οχι**	**Δεν είμαι σίγουρη/ος**	**Ναι**	**Σίγουρα Ναι**
1	Θα ξεκινούσα να γυμνάζομαι επειδή λένε πως πρέπει.	**0**	**1**	**2**	**3**	**4**
2	Θα ξεκινούσα να γυμνάζομαι επειδή αισθάνομαι ενοχές που δεν γυμνάζομαι.	**0**	**1**	**2**	**3**	**4**
3	Θα ξεκινούσα να γυμνάζομαι επειδή εκτιμώ τα οφέλη της γυμναστικής.	**0**	**1**	**2**	**3**	**4**
4	Θα ξεκινούσα να γυμνάζομαι επειδή είναι διασκεδαστικό.	**0**	**1**	**2**	**3**	**4**
5	Δεν βλέπω γιατί πρέπει να γυμνάζομαι.	**0**	**1**	**2**	**3**	**4**
6	Θα ξεκινούσα να γυμνάζομαι επειδή οι άλλοι (φίλοι, οικογένεια, σύντροφος, γιατρός) λένε πως πρέπει.	**0**	**1**	**2**	**3**	**4**
7	Θα ξεκινούσα να γυμνάζομαι επειδή αισθάνομαι άσχημα που δεν το κάνω.	**0**	**1**	**2**	**3**	**4**
8	Θα ξεκινούσα να γυμνάζομαι επειδή είναι σημαντικό για μένα να γυμνάζομαι συστηματικά.	**0**	**1**	**2**	**3**	**4**
9	Δεν βλέπω τον λόγο γιατί θα πρέπει να μπαίνω στον κόπο να γυμνάζομαι.	**0**	**1**	**2**	**3**	**4**
10	Θα ξεκινούσα να γυμνάζομαι επειδή θα το ευχαριστιόμουνα	**0**	**1**	**2**	**3**	**4**

Παράδειγμα:	**Σίγουρα Όχι**	**Όχι**	**Δεν είμαι σίγουρος/η**	**Ναι**	**Σίγουρα ναι**
Θα ξεκινούσα να γυμνάζομαι για να βελτιώσω την υγεία μου.	0	1	2	3	[4]

Θα ξεκινούσα να γυμνάζομαι επειδή ...		**Σίγουρα όχι**	**Οχι**	**Δεν είμαι σίγουρη/ος**	**Ναι**	**Σίγουρα Ναι**
11	Θα ξεκινούσα να γυμνάζομαι επειδή οι άλλοι δεν θα ήταν ευχαριστημένοι μαζί μου εάν δεν το έκανα.	**0**	**1**	**2**	**3**	**4**
12	Δεν βρίσκω νόημα στο να γυμνάζομαι.	**0**	**1**	**2**	**3**	**4**
13	Θα ξεκινούσα να γυμνάζομαι επειδή αισθάνομαι σαν αποτυχία το γεγονός ότι δεν γυμνάζομαι.	**0**	**1**	**2**	**3**	**4**
14	Θα ξεκινούσα να γυμνάζομαι επειδή είναι σημαντικό για μένα να κάνω την προσπάθεια να γυμνάζομαι.	**0**	**1**	**2**	**3**	**4**
15	Θα ξεκινούσα να γυμνάζομαι επειδή θεωρώ ότι η γυμναστική είναι μία ευχάριστη δραστηριότητα.	**0**	**1**	**2**	**3**	**4**
16	Θα ξεκινούσα να γυμνάζομαι επειδή αισθάνομαι πίεση από τους άλλους (φίλοι, οικογένεια, σύντροφος, γιατρός) να γυμνάζομαι.	**0**	**1**	**2**	**3**	**4**
17	Θα ξεκινούσα να γυμνάζομαι επειδή νιώθω γεμάτος ενέργεια που θέλω να εκτονώσω.	**0**	**1**	**2**	**3**	**4**
18	Θα ξεκινούσα να γυμνάζομαι επειδή θα αντλήσω ευχαρίστηση και ικανοποίηση από την γυμναστική.	**0**	**1**	**2**	**3**	**4**
19	Νομίζω πως η γυμναστική είναι χάσιμο χρόνου.	**0**	**1**	**2**	**3**	**4**

C.Σε τι βαθμό οι παρακάτω δηλώσεις ισχύουν για σας αν υποθέσουμε ότι προτίθεστε να συνεχίσετε μακροχρόνια να γυμνάζεστε συστηματικά. Παρακαλώ βάλτε σε κύκλο έναν αριθμό.

1.Αισθάνομαι αυτοπεποίθηση για την ικανότητα μου να γυμνάζομαι συστηματικά

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

2. Αισθάνομαι ικανός-ή να γυμνάζομαι συστηματικά

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

3.Είμαι ικανός-ή να γυμνάζομαι συστηματικά για μεγάλο χρονικό διάστημα

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

4.Είμαι ικανός-ή να ανταποκριθώ στην πρόκληση του να γυμνάζομαι συστηματικά

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

Α.Πώς έχετε αισθανθεί σε συζητήσεις που μπορεί να έχετε κάνει με ειδικούς ή σημαντικούς για εσάς ανθρώπους (όπως π.χ. τον/την γιατρό σας, κάποιον/α γυμναστή/στρια, την οικογένειά σας, τον/την σύντροφό σας, τους φίλους σας) σχετικά με τη γυμναστική; (π.χ., το να γυμνάζεστε, το πόσο συχνά γυμνάζεστε, το πόσο έντονα γυμνάζεστε, τον τρόπο με τον οποίο γυμνάζεστε, κτλ). Παρακαλώ βάλτε σε κύκλο έναν αριθμό.

1.Αισθάνομαι ότι έχω επιλογές σχετικά με το αν θα γυμνάζομαι συστηματικά και με τι τρόπο

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

2. Αισθάνομαι ότι οι άλλοι άνθρωποι κατανοούν το πώς βλέπω τα πράγματα σχετικά με τη γυμναστική

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

3.Αισθάνομαι ότι οι άλλοι εμπιστεύονται την ικανότητα μου να αποφασίζω για τον τρόπο που γυμνάζομαι

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

4. Αισθάνομαι ότι οι άλλοι δίνουν προσοχή στο πώς θέλω να γυμνάζομαι

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

5. Αισθάνομαι ότι οι άλλοι με ενθαρρύνουν να κάνω ερωτήσεις σχετικά με το πώς να γυμνάζομαι

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

6. Αισθάνομαι ότι οι άλλοι άνθρωποι προσπαθούν να κατανοήσουν το πώς βλέπω τη γυμναστική, πριν μου προτείνουν όποια αλλαγή για το πως να γυμνάζομαι

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

R.Πως αισθάνεστε στο χώρο γυμναστικής και με τους ανθρώπους με τους οποίους γυμνάζεστε; Παρακαλώ βάλτε σε κύκλο έναν αριθμό.

1. Αισθάνομαι πάρα πολύ άνετα στις σχέσεις μου με άλλους που γυμνάζονται

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

2. Αισθάνομαι ότι οι σχέσεις μου με άλλους που γυμνάζονται είναι πάρα πολύ φιλικές.

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

3. Αισθάνομαι ότι έχω άριστη επικοινωνία με άλλους που γυμνάζονται

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

4. Αισθάνομαι ότι οι σχέσεις μου με άλλους που γυμνάζονται είναι πάρα πολύ οικείες

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

C. Σε τι βαθμό οι παρακάτω δηλώσεις ισχύουν για σας αν υποθέσουμε ότι προτίθεστε να ξεκινήσετε να γυμνάζεστε συστηματικά. Παρακαλώ βάλτε σε κύκλο έναν αριθμό.

1. Αισθάνομαι αυτοπεποίθηση για την ικανότητα μου να γυμναστώ συστηματικά

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

2. Αισθάνομαι ικανός-ή στο να γυμναστώ συστηματικά

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

3. Είμαι ικανός-ή στο να γυμναστώ συστηματικά για μεγάλο χρονικό διάστημα

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

4. Είμαι ικανός-ή να ανταποκριθώ στην πρόκληση του να γυμναστώ συστηματικά

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

Α.Πώς έχετε αισθανθεί ή θα αισθανόσασταν σε συζητήσεις με ειδικούς ή σημαντικούς για εσάς ανθρώπους (όπως π.χ. τον/την γιατρό σας, κάποιον/α γυμναστή/στρια, την οικογένειά σας, τον/την σύντροφό σας, τους φίλους σας) σχετικά με το ενδεχόμενο να αρχίσετε να γυμνάζεστε; (π.χ., το αν θα γυμνάζεστε, το πόσο συχνά θα γυμνάζεστε, το πόσο έντονα θα γυμνάζεστε, τον τρόπο με τον οποίο θα γυμνάζεστε). Παρακαλώ βάλτε σε κύκλο έναν αριθμό.

1. Αισθάνομαι ότι έχω επιλογές σχετικά με το αν θα γυμνάζομαι συστηματικά και με τι τρόπο

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

2. Αισθάνομαι ότι οι άλλοι κατανοούν το πως βλέπω τα πράγματα σχετικά με το αν γυμνάζομαι

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

3. Αισθάνομαι ότι οι άλλοι εμπιστεύονται την ικανότητα μου να αποφασίσω να αρχίσω να γυμνάζομαι

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

4. Αισθάνομαι ότι οι άλλοι δίνουν προσοχή στο πως θα ήθελα να γυμνάζομαι

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

5. Αισθάνομαι ότι οι άλλοι με ενθαρρύνουν να κάνω ερωτήσεις σχετικά με το πως θα ήθελα να γυμνάζομαι

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

6. Αισθάνομαι ότι οι άλλοι προσπαθούν να κατανοήσουν το πως βλέπω τη γυμναστική, πριν μου προτείνουν να ξεκινήσω να γυμνάζομαι

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

R.Αν ξεκινούσατε να γυμνάζεστε συστηματικά, πώς πιστεύετε ότι θα αισθανόσασταν στον χώρο γυμναστικής και για τους ανθρώπους με τους οποίους θα γυμναζόσασταν; Παρακαλώ βάλτε σε κύκλο έναν αριθμό.

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

2. Αισθάνομαι ότι οι σχέσεις μου με άλλους που γυμνάζονται θα ήταν πάρα πολύ φιλικές

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

3. Αισθάνομαι ότι θα είχα άριστη επικοινωνία με άλλους που γυμνάζονται

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

4. Αισθάνομαι ότι οι σχέσεις μου με άλλους που γυμνάζονται θα ήταν πάρα πολύ οικείες

1	2	3	4	5	6	7
δεν ισχύει καθόλου για μένα			ισχύει κάπως για μένα			ισχύει πάρα πολύ για μένα

Ορισμός **συστηματικής σωματικής δραστηριότητας**:

Η **σωματική δραστηριότητα** περιλαμβάνει ασχολίες όπως γρήγορο περπάτημα, χορό, τρέξιμο, ποδηλασία, κολύμβηση, τένις ή οποιαδήποτε άλλη ασχολία ή άθλημα σε κάνει να κινείσαι, να αναπνέεις πιο γρήγορα, να ιδρώνεις έστω και λίγο και αυξάνει τους χτύπους της καρδιάς σου χωρίς να είναι απαραίτητα κουραστική. Οι δραστηριότητες που μας ενδιαφέρουν είναι αυτές που έχουν είτε **μέτρια ένταση** (όχι ιδιαίτερα κουραστικές) είτε **μεγάλη ένταση** (περισσότερο κουραστικές).

Ένας άνθρωπος της ηλικίας σας για να θεωρείται **συστηματικάσωματικά δραστήριος** θα πρέπει να συμπληρώνει **τουλάχιστον 5 φορές την εβδομάδα από 1 ώραμέτριας** σωματικής δραστηριότητας **ήτουλάχιστον 3 φορές την εβδομάδα από 30 λεπτά έντονης** σωματικής δραστηριότητας ή ένα συνδυασμό δραστηριοτήτων μέτριας και μεγάλης έντασης π.χ. 2 ώρες μέτριας και 1 ώρα έντονης σωματικής δραστηριότητας την εβδομάδα. .

Τα τραντάλεπτα **έντονης** σωματικής δραστηριότητας θα πρέπει να είναι συνεχόμενα. Οι ώρες **μέτριας** σωματικής δραστηριότητας μπορεί να είναι είτε συνεχόμενες, είτε χωρισμένες σε μικρότερα χρονικά διαστήματα κατά τη διάρκεια της ημέρας π.χ. ένα εικοσάλεπτο γρήγορου βαδίσματος το πρωί, ένα δεκάλεπτο ποδηλασίας το απόγευμα και ένα τριαντάλεπτο χορού το βράδυ συμπληρώνουν τα 60 λεπτά σωματικής δραστηριότητας.

Ερώτηση:

Είσαι **συστηματικά σωματικά δραστήριος/α** σύμφωνα με τον παραπάνω ορισμό;

*Διάβασε πρώτα **όλες** τις παρακάτω **απαντήσεις** και μετά σημείωσε με Χ **μόνο μία**, η οποία σε αντιπροσωπεύει.*

☐ Όχι, δεν είμαι συστηματικά σωματικά δραστήριος/α, και δεν σκοπεύω να γίνω στους επόμενους 6 μήνες

☐ Όχι, δεν είμαι συστηματικά σωματικά δραστήριος/α, αλλά σκοπεύω να γίνω στους επόμενους 6 μήνες

☐ Όχι, δεν είμαι συστηματικά σωματικά δραστήριος/α, αλλά σκοπεύω να γίνω στις επόμενες 30 ημέρες

☐ Ναι, είμαι συστηματικά σωματικά δραστήριος/α, αλλά για λιγότερο από έξι μήνες

☐ Ναι, είμαι συστηματικά σωματικά δραστήριος/α για περισσότερο από έξι μήνες

IPAQ Παρακάτω ακολουθούν ερωτήσεις σχετικά με την άσκηση-(γυμναστική)

1. Κατά τη διάρκεια των **τελευταίων 7 ημερών**, πόσες ημέρες συμμετείχατε σε άσκηση-(γυμναστική) **υψηλής έντασης** έτσι ώστε να **αναπνέετε πολύ πιο δύσκολα από ότι συνήθως** τουλάχιστον 10 λεπτά κάθε φορά (π.χ. αερόβια άσκηση, γρήγορη ποδηλασία)

_____ **ημέρες ανά εβδομάδα**

☐Καθόλου υψηλής έντασης άσκηση-(γυμναστική) → **προχωρήστε στην ερώτηση 3**

2. Πόσο χρόνο συνήθως αφιερώσατε για να συμμετέχετε σε άσκηση-(γυμναστική) **υψηλής έντασης** σε μία από αυτές τις ημέρες;

_____ **ώρες την ημέρα**

_____ **λεπτά την ημέρα**

☐Δεν γνωρίζω/ Δεν είμαι σίγουρος/η

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3. Κατά τη διάρκεια των **τελευταίων 7 ημερών**, πόσες μέρες συμμετείχατε σε άσκηση-(γυμναστική) **μέτριας έντασης,** έτσι ώστε **να αναπνέετε λίγο πιο δύσκολα από ότι συνήθως για τουλάχιστον 10 λεπτά** (π.χ. τρέξιμο σε κανονικό ρυθμό). Μην συμπεριλάβετε το περπάτημα.

_____ **ημέρες ανά εβδομάδα**

☐ Καθόλου μέτριας έντασης άσκηση-(γυμναστική)→ **προχωρήστε στην ερώτηση 5**

4. Πόσο χρόνο συνήθως αφιερώσατε για να συμμετέχετεσε άσκηση-(γυμναστική) **μέτριας έντασης** σε μία από αυτές τις ημέρες;

_____ **ώρες την ημέρα**

_____ **λεπτά την ημέρα**

☐Δεν γνωρίζω/ Δεν είμαι σίγουρος/η

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5. Κατά τη διάρκεια των **τελευταίων 7 ημερών**, πόσες ημέρες **περπατήσατε** για τουλάχιστον 10 λεπτά;

_____ **ημέρες ανά εβδομάδα**

☐Καθόλου περπάτημα → **προχωρήστε στην ερώτηση 7**

6. Πόσο χρόνο συνήθως αφιερώσατε **περπατώντας** σε μία από αυτές τις ημέρες;

_____ **ώρες την ημέρα**

_____ **λεπτά την ημέρα**

☐Δεν γνωρίζω/ Δεν είμαι σίγουρος/η

Η τελευταία ερώτηση είναι σχετικά με το χρόνο που **κάθεστε** σε μια συνηθισμένη ημέρα στο διάστημα των **τελευταίων 7 ημερών** (π.χ. ώρα εργασίας, διαβάσματος, παρακολούθησης τηλεόρασης)

7. Κατά τη διάρκεια των **τελευταίων 7 ημερών**, πόσο χρόνο **καθίσατε** σε μια **συνηθισμένη ημέρα της εβδομάδας;**

_____ **ώρες την ημέρα**

_____ **λεπτά την ημέρα**

□Δεν γνωρίζω/ Δεν είμαι σίγουρος/η

Παρακαλώ υποδείξτε σε τι βαθμό βιώσατε τα παρακάτω συναισθήματα **την τελευταία εβδομάδα**.

		ΚΑΘΟΛΟΥ				**ΠΑΡΑ ΠΟΛΥ**
1	Εκνευρισμένος/η	①	②	③	④	⑤
2	Ήρεμος/η	①	②	③	④	⑤
3	Εξαντλημένος	①	②	③	④	⑤
4	Δραστήριος/α	①	②	③	④	⑤
5	Εξοργισμένος/η	①	②	③	④	⑤
6	Χαλαρός/ή	①	②	③	④	⑤
7	Καταπονημένος/η	①	②	③	④	⑤
8	Γεμάτος/η ενέργεια	①	②	③	④	⑤
9	Συγχυσμένος/η	①	②	③	④	⑤
10	Γαλήνιος/α	①	②	③	④	⑤
11	Κουρασμένος/η	①	②	③	④	⑤
12	Δυναμικός/ή	①	②	③	④	⑤
13	Ταραγμένος/η	①	②	③	④	⑤
14	Ήσυχος/η	①	②	③	④	⑤
15	Καταβεβλημένος/η	①	②	③	④	⑤
16	Γεμάτος/η ζωντάνια	①	②	③	④	⑤
17	Νευρικός/ή	①	②	③	④	⑤
18	Ατάραχος/η	①	②	③	④	⑤
19	Εξουθενωμένος/η	①	②	③	④	⑤
20	Ευέξαπτος /η	①	②	③	④	⑤

Η υγεία και η ευημερία σας

Το ερωτηματολόγιο αυτό ζητά τις δικές σας απόψεις για την υγεία σας. Οι πληροφορίες σας θα μας βοηθήσουν να εξακριβώσουμε πώς αισθάνεστε και πόσο καλά μπορείτε να ασχοληθείτε με τις συνηθισμένες δραστηριότητές σας. ***Σας ευχαριστούμε για τη συμπλήρωση αυτού του ερωτηματολογίου!***

Παρακαλούμε, σε κάθε ερώτηση που ακολουθεί σημειώστε με ☒ το πλαίσιο που περιγράφει καλύτερα την απάντησή σας.

1. **Γενικά, θα λέγατε ότι η υγεία σας είναι:**

Άριστη	Πολύ καλή	Καλή	Μέτρια	Κακή
☐1	☐2	☐3	☐4	☐5

2. **Οι παρακάτω προτάσεις περιέχουν δραστηριότητες που μπορεί να κάνατε κατά τη διάρκεια μιας συνηθισμένης ημέρας.Η τωρινή κατάσταση της υγείας σας, σας περιορίζει σε αυτές τις δραστηριότητες; Εάν ναι, πόσο;**

	Ναι, με περιορίζει πολύ	Ναι, με περιορίζει λίγο	Όχι, δεν με περιορίζει καθόλου
a Σε μέτριας έντασης δραστηριότητες, όπως η μετακίνηση ενός τραπεζιού, το σπρώξιμο μιας ηλεκτρικής σκούπας, το κολύμπι ή όταν παίζετε ρακέτες στην παραλία	☐1	☐2	☐3
b Όταν ανεβαίνετε μερικές σειρές από σκαλοπάτια	☐1	☐2	☐3

1. **Τις τελευταίες 4 εβδομάδες, πόσο συχνά είχατε κάποια από τα παρακάτω προβλήματα στη δουλειά σας ή σε άλλες συνηθισμένες καθημερινές δραστηριότητες ως αποτέλεσμα της κατάστασης της σωματικής σας υγείας;**

2. **Τις τελευταίες 4 εβδομάδες, πόσο συχνά είχατε κάποια από τα παρακάτω προβλήματα στη δουλειά σας ή σε άλλες συνηθισμένες καθημερινές δραστηριότητες ως αποτέλεσμα οποιουδήποτε συναισθηματικού προβλήματος (όπως επειδή νοιώσατε μελαγχολία ή άγχος);**

	Συνεχώς	Τις περισσότερες φορές	Μερικές φορές	Λίγες φορές	Καθόλου
a Κάνατε λιγότερα από όσα θα θέλατε	☐1	☐2	☐3	☐4	☐5
b Κάνατε τη δουλειά ή άλλες δραστηριότητεςλιγότερο προσεκτικά απ' ότι συνήθως	☐1	☐2	☐3	☐4	☐5

3. **Τις τελευταίες 4 εβδομάδες, πόσο επηρέασε ο πόνος τη συνηθισμένη εργασία σας (τόσο την εργασία έξω από το σπίτι όσο και μέσα σε αυτό);**

Καθόλου	Λίγο	Μέτρια	Σε μεγάλο βαθμό	Υπερβολικά
☐1	☐2	☐3	☐4	☐5

1. **Οι παρακάτω ερωτήσεις αναφέρονται στο πως αισθανόσαστε και στο πως τα πράγματα πήγαιναν με σας τις τελευταίες 4 εβδομάδες. Για κάθε ερώτηση, παρακαλείστε να δώσετε εκείνη την απάντηση που πλησιάζει περισσότερο σε ό,τι αισθανθήκατε. Τις τελευταίες 4 εβδομάδες, για πόσο χρονικό διάστημα…**

	Συνεχώς	Τις περισσότερες φορές	Μερικές φορές	Λίγες φορές	Καθόλου
	▼	▼	▼	▼	▼
a Αισθανόσασταν ηρεμία και γαλήνη;	☐1	☐2	☐3	☐4	☐5
b Είχατε πολλή ενεργητικότητα;	☐1	☐2	☐3	☐4	☐5
c Αισθανόσασταν κακοκεφιά και μελαγχολία;	☐1	☐2	☐3	☐4	☐5

2. **Τις τελευταίες 4 εβδομάδες, για πόσο χρονικό διάστημα επηρέασαν τις κοινωνικές σας δραστηριότητες (π.χ. επισκέψεις σε φίλους, συγγενείς κλπ.) η κατάσταση της σωματικής σας υγείας ή συναισθηματικά σας προβλήματα;**

Συνεχώς	Τις περισσότερες φορές	Μερικές φορές	Λίγες φορές	Καθόλου
▼	▼	▼	▼	▼
☐1	☐2	☐3	☐4	☐5

Σας ευχαριστούμε για το χρόνο σας!

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